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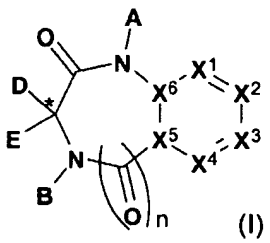
(54) Title: BENZODIAZEPINE AND BENZOPIPERAZINE ANALOG INHIBITORS OF HISTONE DEACETYLASE



(I)

(57) Abstract: This invention relates to compounds for the inhibition of histone deacetylase More particularly, the invention provides for compounds of formula (I): wherein A, B, D, E, X^1, X^2, X^3, X^4 and n are as defined in the specification A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a compound of formula (I), in an amount sufficient to inhibit histone deacetylase, is also disclosed.

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BENZODIAZEPINE AND BENZOPIPERAZINE ANALOG INHIBITORS OF HISTONE DEACETYLASE

BACKGROUND OF THE INVENTION

This application claims the benefit of U.S. provisional application no. 60/712,011, filed August 26, 2005.

(a) Field of the Invention

[0001] This invention relates to the inhibition of histone deacetylase. More particularly, the invention relates to compounds and methods for inhibiting histone deacetylase enzymatic activity.

(b) Description of Related Art

[0002] In eukaryotic cells, nuclear DNA associates with histones to form a compact complex called chromatin. The histones constitute a family of basic proteins which are generally highly conserved across eukaryotic species. The core histones, termed H2A, H2B, H3, and H4, associate to form a protein core. DNA winds around this protein core, with the basic amino acids of the histones interacting with the negatively charged phosphate groups of the DNA. Approximately 146 base pairs of DNA wrap around a histone core to make up a nucleosome particle, the repeating structural motif of chromatin.

[0003] Csordas, *Biochem. J.*, **265**: 23-38 (1990) teaches that histones are subject to post-translational acetylation of the ε-amino groups of *N*-terminal lysine residues, a reaction that is catalyzed by histone acetyl transferase (HAT1). Acetylation neutralizes the positive charge of the lysine side chain, and is thought to impact chromatin structure. Indeed, Taunton *et al.*, *Science,* **272**: 408-411 (1996), teaches that access of transcription factors to chromatin templates is enhanced by histone hyperacetylation. Taunton *et al.* further teach that an enrichment in underacetylated histone H4 has been found in transcriptionally silent regions of the genome.

[0004] Histone acetylation is a reversible modification, with deacetylation being catalyzed by a family of enzymes termed histone deacetylases (HDACs). The molecular cloning of gene sequences encoding proteins with HDAC activity has established the existence of a set of discrete HDAC enzyme isoforms. Grozinger et al., Proc. Natl. Acad. Sci. USA, 96:4868-4873 (1999), teaches that HDACs may be divided into two classes, the first represented by yeast Rpd3-like proteins, and the second represented by yeast Hd1-like proteins. Grozinger et al. also teaches that the human HDAC-1, HDAC-2, and HDAC-3 proteins are members of the first class of HDACs, and discloses new proteins, named HDAC-4, HDAC-5, and HDAC-6, which are members of the second class of HDACs. Kao et al., Gene & Development 14:55-66 (2000), discloses an additional member of this second

class, called HDAC-7. More recently, Hu, E. et al. J. Bio. Chem. 275:15254-13264 (2000) discloses the newest member of the first class of histone deacetylases, HDAC-8. Zhou et al., Proc. Natl. Acad. Sci. U.S.A., 98: 10572-10577 (2001) teaches the cloning and characterization of a new histone deacetylase, HDAC-9. Kao et al., J. Biol. Chem., 277:187-93 (2002) teaches the isolation and characterization of mammalian HDAC10, a novel histone deacetylase. Gao et al, J. Biol. Chem. (**In press**) teaches the cloning and functional characterization of HDAC11, a novel member of the human histone deacetylase family. Shore, Proc. Natl. Acad. Sci. U.S.A. 97: 14030-2 (2000) discloses another class of deacetylase activity, the Sir2 protein family. It has been unclear what roles these individual HDAC enzymes play.

[0005] Studies utilizing known HDAC inhibitors have established a link between acetylation and gene expression. Numerous studies have examined the relationship between HDAC and gene expression. Taunton et al., Science 272:408-411 (1996), discloses a human HDAC that is related to a yeast transcriptional regulator. Cress et al., J. Cell. Phys. 184:1-16 (2000), discloses that, in the context of human cancer, the role of HDAC is as a corepressor of transcription. Ng et al., TIBS 25: March (2000), discloses HDAC as a pervasive feature of transcriptional repressor systems. Magnaghi-Jaulin et al., Prog. Cell Cycle Res. 4:41-47 (2000), discloses HDAC as a transcriptional co-regulator important for cell cycle progression.

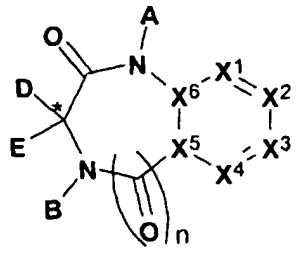
[0006] Richon *et al.*, *Proc. Natl. Acad. Sci. USA*, **95**: 3003-3007 (1998), discloses that HDAC activity is inhibited by trichostatin A (TSA), a natural product isolated from *Streptomyces hygroscopicus*, which has been shown to inhibit histone deacetylase activity and arrest cell cycle progression in cells in the G1 and G2 phases (Yoshida et al., J. Biol. Chem. 265: 17174-17179, 1990; Yoshida et al., Exp. Cell Res. 177: 122-131, 1988), and by a synthetic compound, suberoylanilide hydroxamic acid (SAHA). Yoshida and Beppu, *Exper. Cell Res.*, **177**: 122-131 (1988), teaches that TSA causes arrest of rat fibroblasts at the G_1 and G_2 phases of the cell cycle, implicating HDAC in cell cycle regulation. Indeed, Finnin *et al.*, *Nature*, **401**: 188-193 (1999), teaches that TSA and SAHA inhibit cell growth, induce terminal differentiation, and prevent the formation of tumors in mice. Suzuki *et al.*, U.S. Pat. No. 6,174,905, EP 0847992, and JP 258863/96, disclose benzamide derivatives that induce cell differentiation and inhibit HDAC. WO 03/024448, WO 2004/069823, WO 00/71703, WO 01/38322, WO 01/70675, WO 2004/035525, WO 2005/030705, WO 2005/092899, among others, disclose additional compounds that serve as HDAC inhibitors. Other inhibitors of histone deacetylase activity, including trapoxin, depudecin, FR901228 (Fujisawa Pharmaceuticals), and butyrate, have been found to similarly inhibit cell cycle progression in cells (Taunton et al., Science 272: 408-411, 1996; Kijima et al., J. Biol. Chem. 268(30):22429-22435, 1993; Kwon et al., Proc. Natl. Acad. Sci. USA 95(7):3356-61, 1998).

[0007] It would be highly desirable to be provided with additional compounds and methods for inhibiting histone deacetylase enzymatic activity.

SUMMARY OF THE INVENTION

[0008] The present invention provides compounds for the inhibition of histone deacetylase.

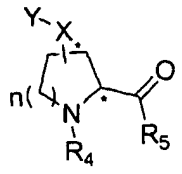
[0009] In a first aspect, the invention provides compounds, and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, that are useful as histone deacetylase inhibitors that have the formula (I):



(I)

wherein A, B, D, E, X^1, X^2, X^3, X^4 and n are as defined below. The compounds are, therefore, also useful research tools for the study of the role of histone deacetylase in both normal and disease states.

[0010] In a second aspect, the invention provides compounds, and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, that are useful as histone deacetylase inhibitiors that have the formula (XVI):



(XVI)

wherein X, Y, R^4, R^5 and n are as defined below. The compounds are, therefore, also useful research tools for the study of the role of histone deceatylase in both normal and disease states.

[0011] In a third aspect, the invention provides a composition comprising a compound according to any one of paragraphs [0009] to [0010], or as depicted in any of the tables herein together with a pharmaceutically acceptable carrier, diluent or excipient.

[0012] In a fourth aspect, the third aspect of the invention provides a method of inhibiting histone deacetylase, the method comprising contacting the histone deacetylase or a cell containing histone deacetylase with a compound according to any one of paragraphs [0009] to [0010] or as depicted in any of the tables herein, or with a composition according to paragraph [0011]. Because compounds of the invention inhibit histone deacetylase, they are useful research tools for the study of the role of histone deacetylase in biological processes.

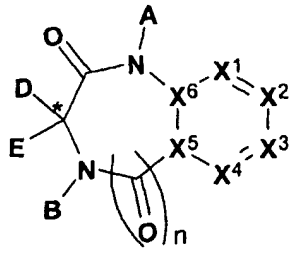
[0013] The foregoing merely summarizes various aspects of the invention and is not intended to be limiting in nature. These aspects and other aspects and embodiments are described more fully below. The patent and scientific literature referred to herein establishes knowledge that is available to those with skill in the art. The issued patents, applications, and references that are cited herein are hereby incorporated by reference to the same extent as if each was specifically and individually indicated to be incorporated by reference. In the case of inconsistencies, the present disclosure will prevail.

[0014] Throughout the specification, preferred embodiments of one or more chemical substituents are identified. Also preferred are combinations of preferred embodiments. For example, the invention describes preferred embodiments of E in the compounds and describes preferred embodiments of group A. Thus, as an example, also contemplated as within the scope of the invention are compounds in which preferred examples of E are as described and in which preferred examples of group A are as described. Furthermore, compounds excluded from any one particular genus of compounds (*e.g.*, through a proviso clause) are intended to be excluded from the scope of the invention entirely, including from other disclosed genera, unless expressly stated to the contrary.

DETAILED DESCRIPTION OF THE INVENTION

[0015] The present invention provides compounds that are useful as inhibitors of histone deacetylase.

[0016] In one aspect of the present invention there is provided compounds of formula (I):



(I)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof,, wherein

n is 0 or 1;

X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, C-Z and N, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z;

X^5-X^6 is C=C;

or

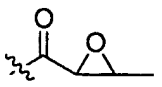
X^1, X^2, X^3 and X^4 are absent, X^5 is a covalent bond and X^6 is independently selected from the group consisting of CH_2 and CH(Z), with the provisio that an N, O or $S(O)_{0-1}$ in Z is separated from the CH of X^6 by at least $-(CH_2)_2-$;

Z is independently selected from the group consisting of halo, $-CF_3$, $-NO_2$, -CN, $-(C_0-C_6)$alkyl-OR^1, $-(C_0-C_6)$alkyl-$N(R^1)_2$, $-(C_1-C_6)$alkyl, $-N(R^1)-C(O)-(C_1-C_6)$alkyl, $-N(R^1)-S(O)_2-(C_1-C_6)$alkyl, $-O-(C_2-C_6)$alkyl-$N(R^1)(R^1)$, $-S-R^1$, $-(C_0-C_6)$alkyl-$C(O)-OR^1$, $-N(R^1)-C(O)-CF_3$, $-N(R^1)-(C_2-C_6)$alkyl-$N(R^1)(R^1)$, $-(C_0-C_7)$alkyl-W, $-(C_2-C_7)$alkenyl-W, $-(C_2-C_7)$alkynyl-W, $-(C_0-C_5)$alkyl-CH=CH-W, $-C(O)-(C_1-C_7)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(S)-(C_1-C_6)$alkyl-W, $-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-O-(C_1-C_6)$alkyl-W, $-S(O)_2-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-S(O)_2-(C_1-C_6)$alkyl-W, $-C(O)-N(R^1)_2$, $-(C_0-C_3)$alkyl-$O-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$O-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$S-(C_1-C_6)$alkyl-W, $-N(R^1)-C(O)-OR^1$, $-S(O)_2-N(R^1)_2$, $-N(R^1)-S(O)_2R^1$, $-(C_0-C_7)$alkyl-aryl-W, $-(C_0-C_7)$alkyl-heteroaryl-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-aryl, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-heteroaryl, -aryl, $-(C_1-C_6)$alkylaryl-, -heteroaryl, $-(C_1-C_6)$alkylheteroaryl-, $-(C_1-C_8)$heteroalkyl, $-(C_3-C_6)$cycloalkyl, $-(C_3-C_6)$heterocycloalkyl, $-(C_0-C_3)$alkyl-$N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-O-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S(O)_2N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)S(O)_2-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-(CH=CH)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-O-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$OC(O)N(R^1)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S(O)_2N(R_1)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)S(O)_2-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$C(O)N(R^1)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)N(R^1)-(C_0-C_3)$alkyl-heteroaryl-$(CH=CH)_{0-1}$-W and $-(C_0-C_3)$alkyl-(CH=CH)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_5)$alkyl-C≡C-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-O-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S(O)_2N(R^1)-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)S(O)_2-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-(C≡C)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-(CH=CH)-(C_0-C_3)alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-(C≡C)-(C_0-C_3)alkyl-aryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)-(C_0-C_3)$alkyl-heteroaryl-$(C\equiv C)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-

heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-S-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-O-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-OC(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-S(O)$_2$N(R_1)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)S(O)$_2$-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-heteroaryl-(CH=CH)$_{0-1}$-W, -(C_0-C_3)alkyl-(CH=CH)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, (C_0-C_3)alkyl-C(O)-N(R^1)-(C_1-C_6)alkyl-W, (C_0-C_3)alkyl-C(S)-N(R^1)-(C_1-C_6)alkyl-W, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-aryl, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-heteroaryl, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-N(R_1)-aryl and -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-N(R_1)-heteroaryl, wherein each of the aryl, heteroaryl, cycloalkyl and heterocyclyl moieties of the above-mentioned Z is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, -SH, mono- to per-halogenated -(C_1-C_6)alkyl, and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group;

R^1 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein each aryl, heteroaryl, cycloalkyl and heterocyclyl moiety of said -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, aryl, heteroaryl, mono- to per-halogenated-(C_1-C_6)alkyl and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group;

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-C_1-C_4 alkyl, -C(O)-N(R^1)$_2$, -(C_1-C_6)alkyl-N(OH)-C(O)H-, -(C_1-C_6)alkyl-SR^1, -(C_1-C_6)alkyl-S-C(O)-(C_1-C_4)alkyl, -C(O)-OR^1,



-C(O)-(C_1-C_4)alkyl-SH, -C(O)-(C_1-C_4)alkyl-S-C(O)R^1, -C(O)-(C_1-C_4)alkyl-S-heteroaryl, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6) alkyl-halo, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SH, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SC(O)R^1, -C(O)-NH-(C_2-C_6)alkyl-SH, -C(O)-N(R^1)-(C_0-C_6)alkyl-SR^1, -C(O)-cycloalkyl, -C(O)-heterocyclyl, -C(O)-N(R^1)-aryl-Q, -C(O)-N(R^1)-heteroaryl-Q, -C(O)-aryl, -C(O)-heteroaryl and -C(O)-(C_1-C_6) alkyl wherein the alkyl is

optionally substituted with one or more substituents selected from the group consisting of halo, mono to per-halogenated-(C_1-C_6)alkyl, -C(O)-heteroaryl, -C(O)-NH-heteroaryl and -C(O)-NH-aryl, wherein each aryl and heteroaryl moiety of the afore-mentioned W group is optionally substituted with one or more substituents selected from the group consisting of $-NH_2$, -OH, -SH, -CN, $-NO_2$, $-N(R^1)_2$, halo, mono- to per-halogenated -(C_1-C_6)alkyl, aryl and heteroaryl;

E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-(C_3-C_6)cycloalkyl, -(C_0-C_6)heteroalkyl-(C_3-C_6)cycloalkyl, -(C_0-C_6)alkyl-(C_3-C_6)heterocyclyl, -(C_0-C_6)heteroalkyl-(C_3-C_6)heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)alkyl-heteroaryl-(C_0-C_3)alkyl-aryl, -(C_0-C_6)alkyl-aryl-(C_0-C_3)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl-(C_0-C_3)alkyl-heteroaryl, -(C_0-C_6)alkyl-aryl-(C_0-C_3)alkyl-heteroaryl, heterocyclyl, -(C_1-C_6)alkyl-S-R^1, -(C_1-C_6)heteroalkyl-S-R^1, -(C_1-C_6)alkyl-O-R^1, -(C_1-C_6)heteroalkyl-O-R^1, -C_1-C_6 alkyl-W, -(C_1-C_6)heteroalkyl-W, -(C_1-C_6)alkyl-M-(C_1-C_3)alkyl-W, -(C_1-C_6)heteroalkyl-M-(C_1-C_3)alkyl-W, -(C_1-C_6)alkyl-$N(R^1)_2$, -(C_1-C_6)heteroalkyl-$N(R^1)_2$, -(C_1-C_6)alkyl-$N(R^1)$-C(O)-OR^1, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)alkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)heteroalkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)alkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)cycloalkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)cycloalkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)heterocyclyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)heterocyclyl, -(C_0-C_6)alkyl-C(O)-$N(R^1)_2$, -(C_0-C_6)heteroalkyl-C(O)-$N(R^1)_2$ and -C(O)-$N(R^1)$-C_2-C_6alkyl-W, wherein each aryl, heteroaryl, cycloalkyl or heterocyclyl moiety is optionally substituted with one or more groups selected from R^2; wherein

M is selected from the group consisting of CH_2, O, S, S(O), $S(O)_2$, and $N(R^1)$; or

C and D together with the carbon atom to which they are attached form a (C_3-C_6)cycloalkyl, wherein the cycloalkyl is optionally substituted;

R^2 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-OR^1, -(C_0-C_6)heteroalkyl-OR^1, -(C_0-C_6)alkyl-C(O)-OR^1, -(C_0-C_6)heteroalkyl-C(O)-OR^1, -CH=CH-C(O)-OR^1, -C≡C-C(O)-OR^1, -CH=CH-C(O)-$N(R^1)_2$, -C≡C-C(O)-$N(R^1)_2$, -$N(R^1)$-C(O)-CF_3, -C(O)-$N(R^1)$-CF_3, -$N(R^1)$-(C_1-C_6)alkyl-$N(R^1)_2$, -$N(R^1)$-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -(C_0-C_6)alkyl-$N(R^1)_2$, -(C_0-C_6)heteroalkyl-$N(R^1)_2$, -$N(R^1)$-C(O)-(C_1-C_6)alkyl, -C(O)-$N(R^1)$-(C_1-C_6)alkyl, -$N(R^1)$-C(O)-(C_1-C_6)heteroalkyl, -C(O)-$N(R^1)$-(C_1-C_6)heteroalkyl, -$N(R^1)$-$S(O)_2$-(C_1-C_6)alkyl, -$N(R^1)$-$S(O)_2$-(C_1-C_6)heteroalkyl, -$S(O)_2$-$N(R^1)$-(C_1-C_6)alkyl, -$S(O)_2$-$N(R^1)$-(C_1-C_6)heteroalkyl, -O-(C_1-C_6)alkyl-$N(R^1)_2$, -O-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -S-(C_1-C_6)alkyl-$N(R^1)_2$, -S-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -S-R^1, -S(O)-(C_1-C_6)alkyl, -S(O)-(C_1-C_6)heteroalkyl, -$S(O)_2$-(C_1-C_6)alkyl, -$S(O)_2$-(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, halo, $-CF_3$, $-OCF_3$, $-C(Ph)_3$, -CN, -(C_1-C_6)alkylaryl, aryl, heteroaryl, -(C_1-C_6)alkylheteroaryl, -(C_1-C_6)heteroalkylaryl, -(C_1-C_6)heteroalkylheteroaryl,

and -(C_1-C_6)alkyl substituted with a moiety selected from the group consisting of halo, -OH, -NO_2, -(C_0-C_6)alkyl-C(O)-N(R^1)$_2$ and -(C_0-C_6)heteroalkyl-C(O)-N(R^1)$_2$;

A and B are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)heteroalkyl-aryl, -(C_0-C_6)hetroalkyl-heteroaryl, -S(O)$_2$-(C_0-C_6)alkyl-aryl, -S(O)$_2$-(C_0-C_6)alkyl-heteroaryl, -S(O)$_2$-(C_0-C_6)heteroalkyl-aryl, -S(O)$_2$-(C_0-C_6)heteroalkyl-heteroaryl, -C(O)-(C_1-C_6)alkyl-aryl, -C(O)-(C_1-C_6)alkyl-heteroaryl, -C(O)-(C_1-C_6)heteoralkyl-aryl, -C(O)-(C_1-C_6)heteroalkyl-heteroaryl, -C(O)O-(C_0-C_6)alkyl-aryl, -C(O)O-(C_1-C_6)alkyl-heteroaryl, -C(O)O-(C_1-C_6)heteroalkyl-aryl, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl, -C(O)N(R^1)-(C_1-C_6)alkyl-aryl, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-aryl, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl, -(C_2-C_6)alkyl-N(R^1)$_2$, -(C_2-C_6)heteroalkyl-N(R^1)$_2$, -(C_2-C_6)alkyl-O(R^1), -(C_2-C_6)heteroalkyl-O(R^1), -(C_1-C_7)alkyl-W, -(C_1-C_7)heteoralkyl-W, -(C_2-C_5)alkyl-(CH=CH)$_{0-1}$-W, -(C_2-C_5)heteroalkyl-(CH=CH)$_{0-1}$-W, -(C_2-C_5)alkyl-(C≡C)$_{0-1}$-W, -(C_2-C_5)heteroalkyl-C≡C-W, -C(O)-(C_1-C_7)alkyl-W, -C(O)-(C_1-C_7)heteroalkyl-W, -S(O)$_2$-(C_1-C_6)alkyl-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-W, -(C_0-C_7)alkyl-aryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-aryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)alkyl-aryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-aryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)alkyl-heteroaryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-heteroaryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)alkyl-aryl-(C_0-C_4)alkyl-W, -(C_0-C_7)heteroalkyl-aryl-(C_0-C_4)alkyl-W, -(C_0-C_7)alkyl-aryl-(C_0-C_4)heteroalkyl-W, -(C_0-C_7)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-W, -(C_0-C_7)alkyl-heteroaryl-(C_0-C_4)alkyl-W, -(C_0-C_7)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-W, -(C_0-C_7)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-W, -(C_0-C_7)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-W, -S(O)$_2$-(C_1-C_6)alkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C_1-C_6)alkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C_1-C_6)alkyl-aryl-(C_0-

C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W , -C(O)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W , -C(O)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W , -C(O)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W , -C(O)O-(C_0-C_6)alkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_0-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_0-C_6)alkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_0-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_0-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_0-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_0-C_6)alkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_0-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)alkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W and -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W;

wherein each of the alkyl and heteroalkyl moieties is optionally substituted; and

wherein each of the aryl, heteroaryl, cycloalkyl or heterocyclyl moieties is optionally substituted with one or more groups selected from R^2; and

the asterick mark * indicates a chiral carbon atom,

with the proviso that no more than two of Z, A, B, D and E end with the moiety W.

[0017] In a preferred embodiment of Formula (I) of the present invention, Embodiment A, n is 0.

[0018] In another preferred embodiment of Formula (I) of the present invention, Embodiment B, n is 1.

[0019] In another preferred embodiment of Formula (I) of the present invention, Embodiment C, X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH and C-Z, wherein no more than one of X^1, X^2, X^3 and X^4 are C-Z.

[0020] In another preferred embodiment of Formula (I) of the present invention, Embodiment D, X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, N and C-Z, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z, wherein Z is selected from the group consisting of -H, halo, -CF_3, -NO_2, -CN, -$(C_0$-$C_6)$alkyl-OR^1, -$(C_0$-$C_6)$alkyl-$N(R^1)_2$, -$(C_1$-$C_6)$alkyl, -$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl, -$N(R^1)$-$S(O)_2$-$(C_1$-$C_6)$alkyl, -O-$(C_2$-$C_6)$alkyl-$N(R^1)(R^1)$, -S-R^1, -$(C_0$-$C_6)$alkyl-C(O)-OR^1, -$N(R^1)$-C(O)-CF_3 or -$N(R^1)$-$(C_2$-$C_6)$alkyl-$N(R^1)(R^1)$, -$(C_0$-$C_7)$alkyl-W, -C(O)-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl-C(O)-aryl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl-C(O)-heteroaryl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl-C(O)-$N(R^1)$-aryl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-C(O)-$(C_1$-$C_6)$alkyl-C(O)-$N(R^1)$-heteroaryl, -$(C_0$-$C_7)$alkyl-aryl-W, -$(C_0$-$C_6)$alkyl-OR^1, -$N(R^1)$-C(O)-OR^1, wherein each of the aryl, heteroaryl, cycloalkyl and heterocyclyl moieties of the above-mentioned Z is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -$(C_1$-$C_6)$alkyl, -$(C_1$-$C_6)$alkoxy, -NO_2, -$N(R^1)_2$, halo, -SH, mono- to per-halogenated-$(C_1$-$C_6)$alkyl and -$(C_2$-$C_4)$alkyl-$N(R^1)_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group.

[0021] In another preferred embodiment of Formula (I) of the present invention, Embodiment E, X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, C-Z and N, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z, wherein Z is selected from the group consisting of -F, -Cl, -Br, CF_3, NO_2, -CN, -OR^1, -NR^1R^1, -$(CH_2)_{0\text{-}4}OR^1$, -$(CH_2)_{0\text{-}4}N(R^1)_2$, -$CH_2OH$, -$CH_3$, -$N(R^1)C(O)CH_3$, -$N(R^1)SO_2CH_3$, -$O(CH_2)_{2\text{-}4}N(R^1)(R^1)$, -$SR^1$, -$(CH_2)_{0\text{-}4}C(O)OR^1$, -$N(R^1)C(O)CF_3$ and -$N(R^1)(CH_2)_2N(R^1)(R^1)$, wherein two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl group.

[0022] In another preferred embodiment of Formula (I) of the present invention, Embodiment F, X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH and C-Z, wherein only one of X^1, X^2, X^3 and X^4 are C-Z, and wherein Z is selected from the group consisting of -H, -$(C_0$-$C_7)$alkyl-W, -$(C_0$-$C_5)$alkyl-CH=CH-W, -$(C_0$-$C_5)$alkyl-C≡C-W, -

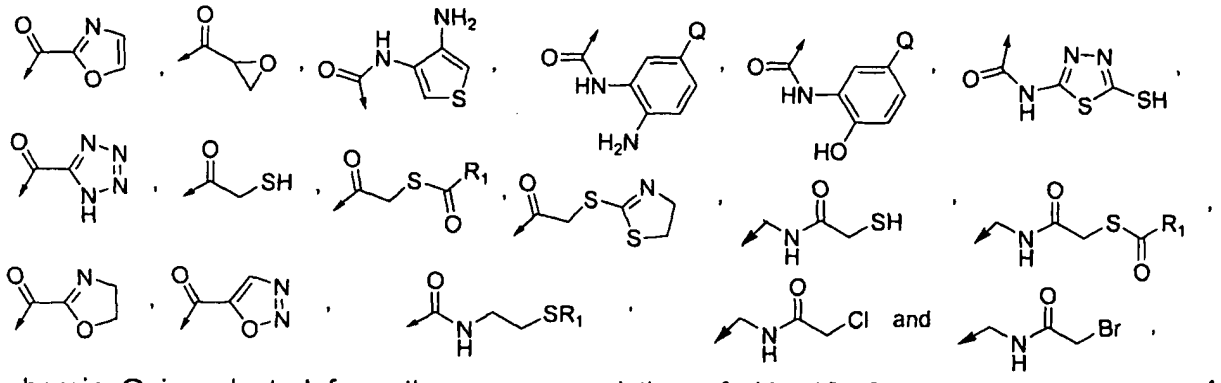
$C(O)$-$(C_1$-$C_7)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(S)$-$(C_1$-$C_6)$alkyl-W, -$C(O)$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$C(S)$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(S)$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-O-$(C_1$-$C_6)$alkyl-W, -$S(O)_2$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$S(O)_2$-$(C_1$-$C_6)$alkyl-W, -O-$C(O)$-$N(R^1)_2$, -$(C_0$-$C_6)$alkyl-O-$C(O)$-$N(R^1)$-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-O-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-S-$(C_1$-$C_6)$alkyl-W, -$N(R^1)$-$C(O)$-O-$S(O)_2$-$N(R^1)_2$, -$N(R^1)$-$S(O)_2$-R^1, -$(C_0$-$C_7)$alkyl-aryl-W, -$(C_0$-$C_7)$alkyl-heteroaryl-W, -$(C_0$-$C_3)$alkyl-O-$(C_0$-$C_3)$alkyl-aryl, -$(C_0$-$C_3)$alkyl-O-$(C_0$-$C_3)$alkyl-heteroaryl, -aryl, -$(C_1$-$C_6)$alkylaryl, -heteroaryl, -$(C_1$-$C_6)$alkylheteroaryl, -$(C_1$-$C_8)$heteroalkyl, -$(C_3$-$C_6)$cycloalkyl, -$(C_3$-$C_6)$heterocycloalkyl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$(C_1$-$C_6)$alkyl-$C(O)$-aryl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$(C_1$-$C_6)$alkyl-$C(O)$-heteroaryl, -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$(C_1$-$C_6)$alkyl-$C(O)$-$N(R^1)$-aryl and -$(C_0$-$C_3)$alkyl-$N(R^1)$-$C(O)$-$(C_1$-$C_6)$alkyl-$C(O)$-$N(R^1)$-heteroaryl, wherein two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl group.

[0023] In another preferred embodiment of Formula (I) of the present invention, Embodiment G, R^1 is independently -$(C_0$-$C_6)$alkyl-aryl or -$(C_1$-$C_4)$alkyl.

[0024] In another preferred embodiment of Formula (I) of the present invention, Embodiment H, R^1 is independently selected from the group consisting of phenyl, benzyl, methyl, ethyl, *t*-butyl and *i*-propyl.

[0025] In another preferred embodiment of Formula (I) of the present invention, Embodiment I, Z is -$(C_2$-$C_4)$alkyl-$N(R^1)_2$, and the two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl selected from the group consisting of morpholinyl, piperazinyl, piperidinyl, pyrrolydinyl, and azetidinyl.

[0026] In another preferred embodiment of Formula (I) of the present invention, Embodiment J, W is selected from the group consisting of



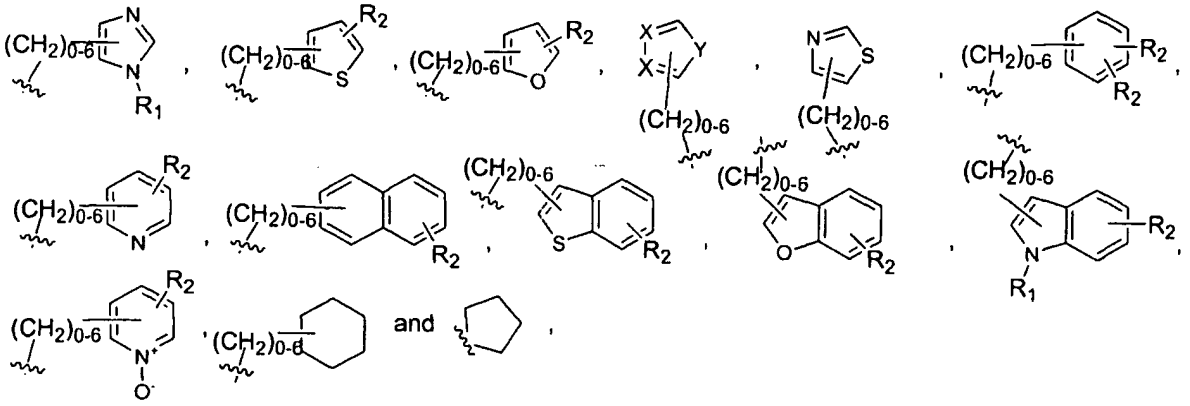
wherein Q is selected from the group consisting of -H, -$(C_1$-$C_6)$alkyl, -$(C_0$-$C_6)$alkyl-OR^1, heterocyclyl, -$N(R^1)_2$, halo, aryl and heteroaryl.

[0027] In another preferred embodiment of Formula (I) of the present invention, Embodiment K, W is selected from the group consisting of -C(O)-NH-OH, $-COCF_3$, $-COCHF_2$, $-COCH_2F$, $-C(O)CH_3$, $-C(O)C_2H_5$, $-(CH_2)_{1-6}$-N(OH)C(O)H and $-CON(R^1)_2$.

[0028] In another preferred embodiment of Formula (I) of the present invention, Embodiment L, Q is independently selected from the group consisting of heterocyclyl, aryl and heteroaryl.

[0029] In another preferred embodiment of Formula (I) of the present invention, Embodiment M, Q is independently selected from the group consisting of thiophenyl, furanyl, tetrazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrrolyl, thiazolyl, oxazolyl and isooxazolyl.

[0030] In another preferred embodiment of Formula (I) of the present invention, Embodiment N, E and D are independently selected from the group consisting of -H, $-(C_1$-$C_6)$alkyl, $-(C_1$-$C_6)$heteroalkyl, $-(C_1$-$C_6)$alkyl-OR^1, $-(C_1$-$C_6)$alkyl-$C(O)$-$N(R^1)_2$, $-(C_1$-$C_6)$alkyl-$C(O)$-O-$(C_1$-$C_6)$alkyl,



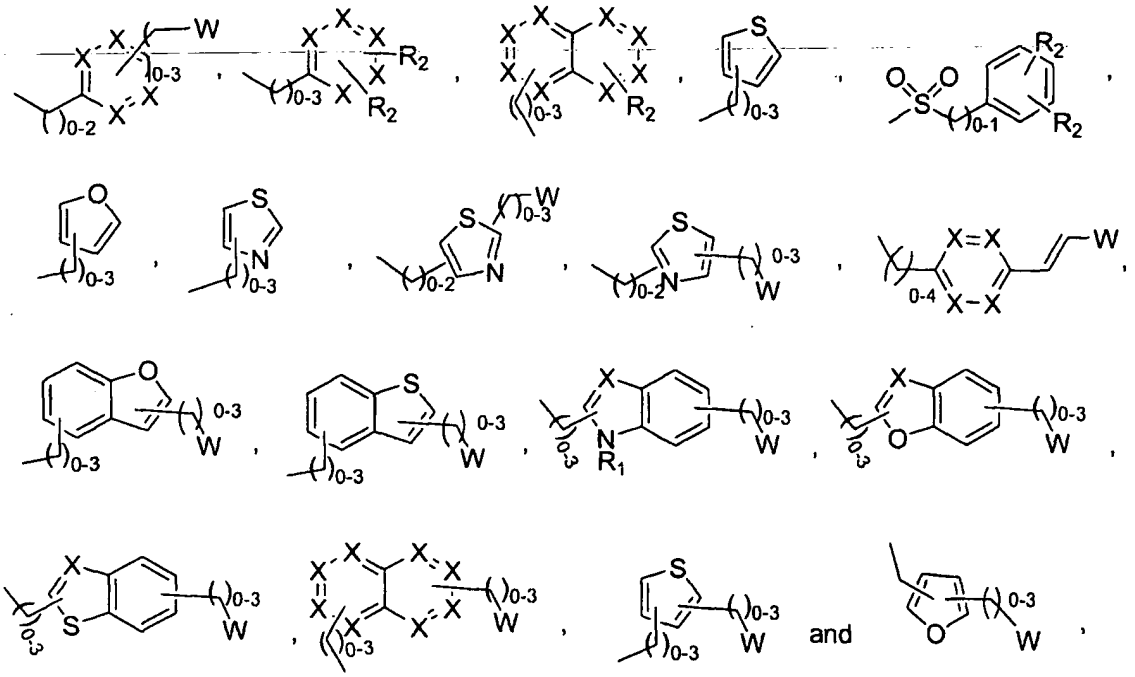
wherein Y is selected from the group consisting of -O-, $-NR^1$-, and -S-, and X is -CH- or -N-.

[0031] In another preferred embodiment of Formula (I) of the present invention, Embodiment O, E and D together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl wherein the cycloalkyl is optionally substituted.

[0032] In another preferred embodiment of Formula (I) of the present invention, Embodiment P, R^2 is independently selected from the group consisting of -H, $-CH_3$, $-OR_1$, $-(CH_2)_{0-4}N(R_1)_2$, -F, -Cl, -Br, $-OCF_3$, $-CF_3$, $-C(Ph)_3$, NO_2, alkyl, aryl, heteroaryl, SR_1 and -CN.

[0033] In another preferred embodiment of Formula (I) of the present invention, Embodiment Q, A and B are independently selected from the group consisting of -H, $-(C_1$-$C_6)$alkyl, heteroalkyl, $-(C_3$-$C_6)$cycloalkyl, heterocycle, $-(C_0$-$C_3)$alkyl-aryl, $-(C_0$-$C_3)$alkyl-heteroaryl, $-(CH_2)_{1-5}$-W, $-S(O)_2$-$(CH_2)_{0-5}$-aryl, $-S(O)_2$-$(CH_2)_{0-5}$-heteroaryl and $-C(O)$-R^2, wherein each of the alkyl and heteroalkyl moieties is optionally substituted; and wherein each of the aryl and heteroaryl moieties is optionally substituted with one or more moieties selected from the group consisting of $-(C_0$-$C_6)$alkyl-aryl, $-(C_0$-$C_6)$alkyl-heteroaryl, $-(C_1$-$C_6)$alkyl, halo, -OH, $-O$-$(C_1$-$C_6)$alkyl, $-C(O)OH$, $-C(O)$-NH-OH.

[0034] In another preferred embodiment of Formula (I) of the present invention, Embodiment R, A and B are independently selected from the group consisting of -H,



wherein X is -CH- or -N-.

[0035] In another preferred embodiment of Formula (I) of the present invention, Embodiment S,

X^1, X^3 and X^4 are CH;

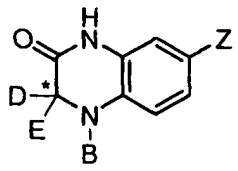
X^2 is C-Z;

n is 0; and

A is -H,

with the proviso that one of E or D is H.

[0036] Another preferred embodiment of Formula (I) of the present invention, Embodiment T, provides compounds of Embodiment S according to the formula (II)



(II)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof,wherein

Z is selected from the group consisting of -H, $-C(O)-N(R^1)_2$, $-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_7)$alkyl-W, $-(C_2-C_7)$alkenyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-(C_1-C_6)$alkyl-W and $-(C_0-C_7)$alkyl-aryl-W;

B is selected from the group consisting of -H, $-S(O)_2-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-heteroaryl and $-(C_0-C_7)$alkyl-aryl-$(CH=CH)_{0-1}$-W; and

E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)alkyl-W, -(C_0-C_6)alkyl-C(O)-N(R^1)$_2$, wherein each of the aryl and heteroaryl is optionally substituted with one or more groups selected from R^2,

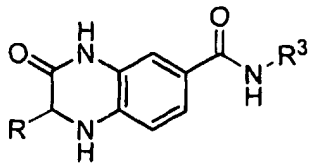
with the proviso that one of E and D is -H.

[0037] In a preferred embodiment of Embodiment T of the present invention, Embodiment U,

Z is selected from the group consisting of -C(O)-N(R^1)$_2$, -C(O)-N(R^1)-(C_1-C_6)alkyl-W; and

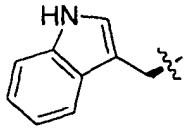
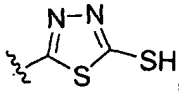
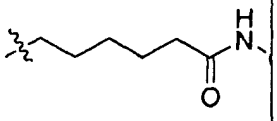
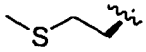
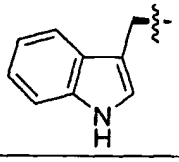
B is -H.

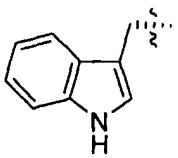
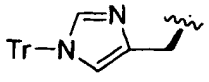
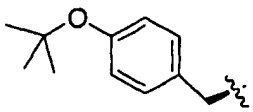
[0038] Another preferred embodiment of Formula (I) of the present invention, Embodiment V, provides compounds according to the formula (III)

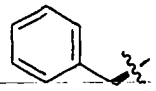
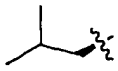
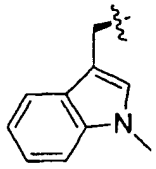
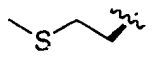
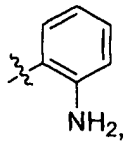


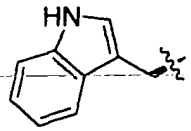
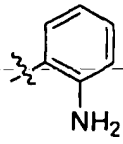
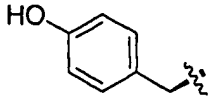
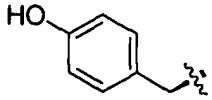
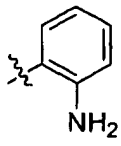
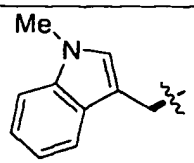
(III)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein R and R^3 are a combination selected from the group consisting of:

R	R^3
	
	
	-OH,
	-OH,
	-OH,

R	R^3
	-OH,
	-OH,
	-OH,
	-OH,
	-OH,

R	R^3
	-OH,
H	-OH,
	-OH,
	-OH,
	

R	R^3
	
	-OH,
	
	-OH.

[0039] In another preferred embodiment of Formula (I) of the present invention, Embodiment W,

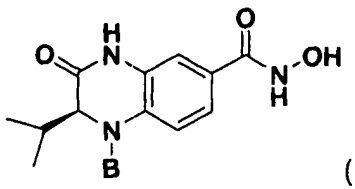
Z is -C(O)-NH-OH;

B is selected from the group consisting of $-S(O)_2-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-heteroaryl, each of which is optionally substituted and $-(C_0-C_7)$alkyl-aryl-$(CH=CH)_{0-1}$-W; and

E and D are independently selected from the group consisting of -H and $-(C_1-C_6)$alkyl, wherein the alkyl moiety is optionally substituted,

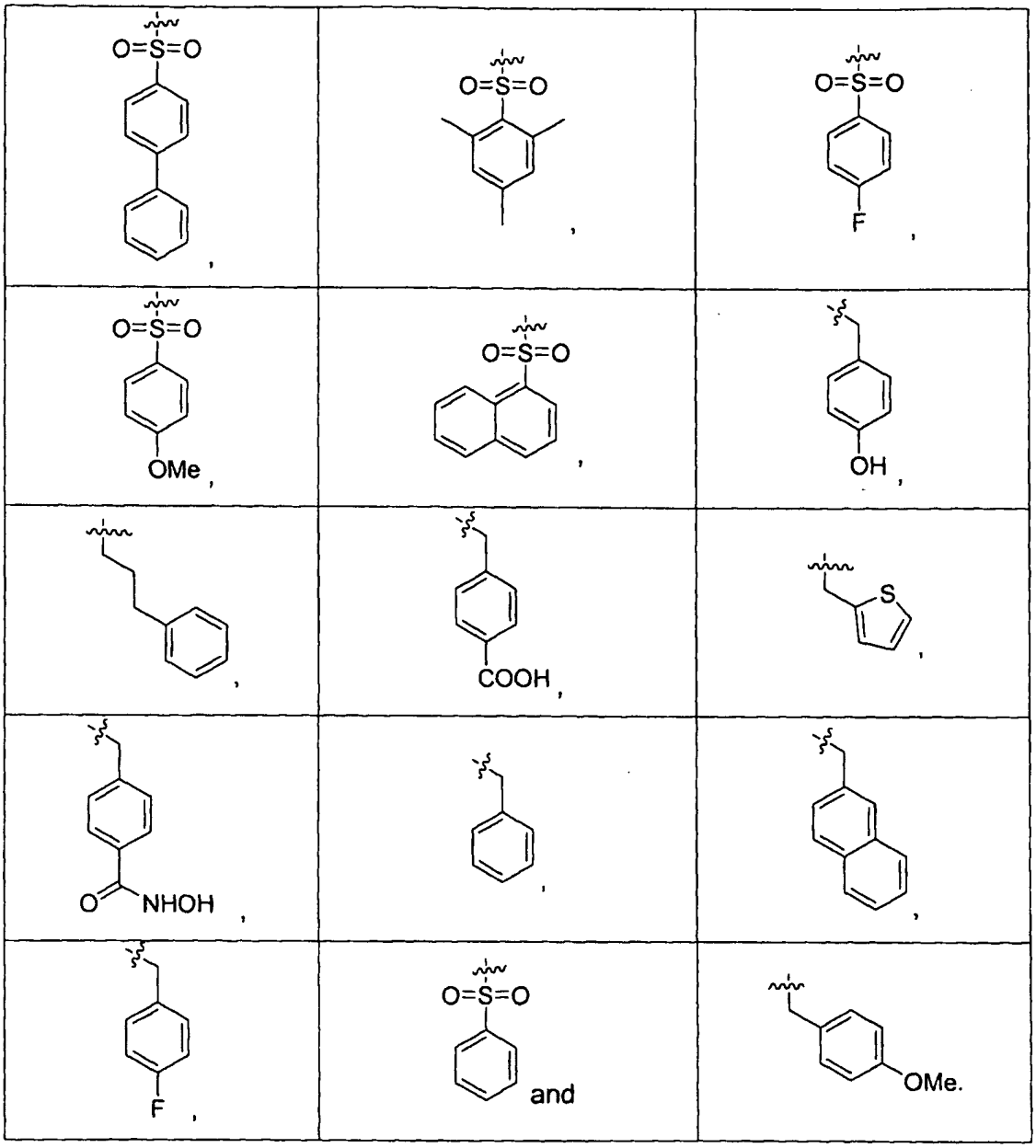
with the proviso that one of C and D is -H.

[0040] Another preferred embodiment of Embodiment T of the present invention, Embodiment X, provides compounds according to the formula (IV)



(IV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B is selected from the group consisting of



[0041] In another preferred embodiment of Formula (I) of the present invention, Embodiment Y,

n is 0;

X^1, X^3 and X^4 are CH;

X^2 is C-Z;

Z is -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-W;

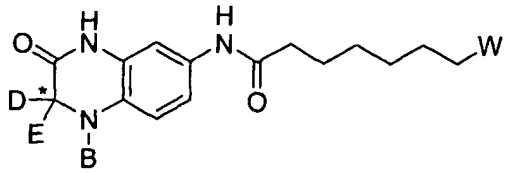
W is selected from the group consisting of -C(O)-NH-OH, -C(O)-heteroaryl, -C(O)-aryl, -C(O)-OR^1, -C(O)-N(R^1)$_2$ and -C(O)-alkyl, wherein the aryl and heteroaryl moieties of said W are optionally substituted;

A is -H;

B is -H or -(C_0-C_6)alkyl-aryl, wherein the aryl moiety is optionally substituted with one or more groups selected from R^2; and

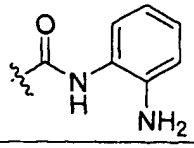
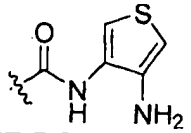
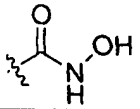
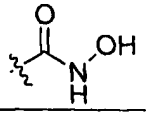
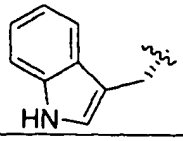
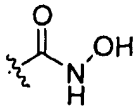
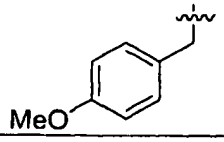
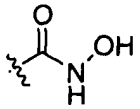
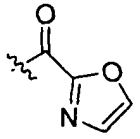
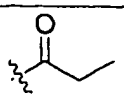
E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl and -(C_0-C_6)alkyl-heteroaryl, wherein the heteroaryl moiety is optionally substituted, with the proviso that at least one of E and D are -H.

[0042] A preferred embodiment of Embodiment X of the present invention, Embodiment Z, provides compounds according to the formula (V)



(V)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of B, E, D and W is selected from the group consisting of

B	E	D	W
H		H	
H		H	
H		H	
H	H		
H	H		
	H		
H		H	
H		H	

[0043] In another preferred embodiment of Formula (I) of the present invention, Embodiment AA,

n is 0;

X^1, X^2, X^3 and X^4 are CH;

A is H;

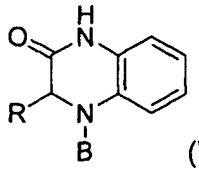
B is selected from the group consisting of -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-aryl-(CH=CH)$_{0-1}$-W, wherein the W moiety is optionally *meta* or *para* to the -(C_0-C_6)alkyl moiety, and wherein the aryl moiety of each of the aforementioned B is optionally substituted with one or more substitutents selected from R^2;

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-NH-aryl, wherein the aryl is optionally substituted,

E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl-M-(C_1-C_3)alkyl-W, -(C_0-C_6)alkyl-C(O)-N(R^1)$_2$, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)alkyl-aryl and -(C_1-C_6)alkyl-N(R^1)-C(O)-OR^1; and

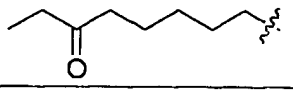
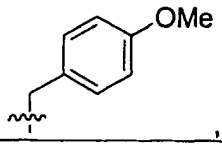
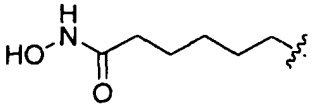
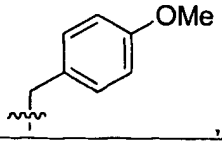
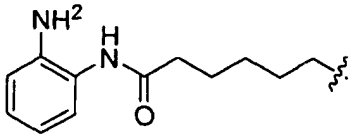
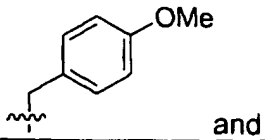
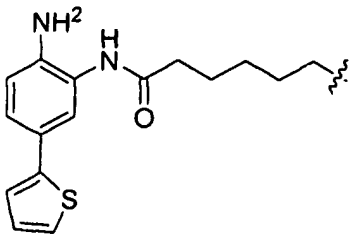
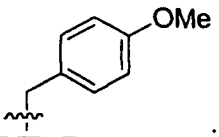
R^1 is independently selected from the group consisting of -H and -(C_1-C_6)alkyl.

[0044] A preferred embodiment of Embodiment AA of the present invention, Embodiment BB, provides compounds according to the formula (VI)

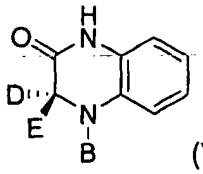


(VI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B and R are a combination selected from the group consisting of

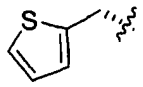
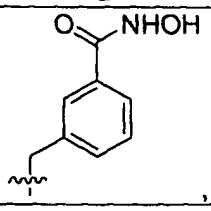
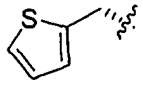
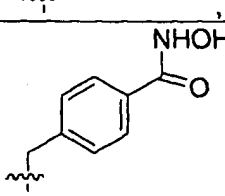
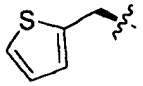
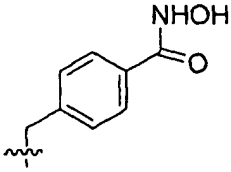
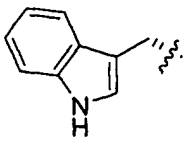
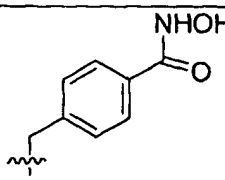
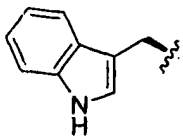
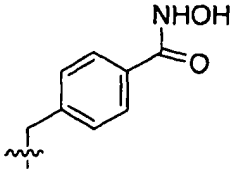
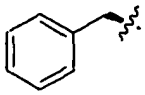
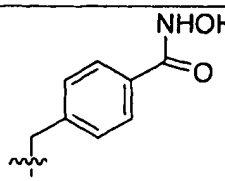
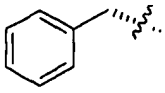
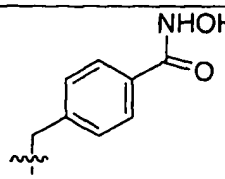
R	B
	
	
	 and
	

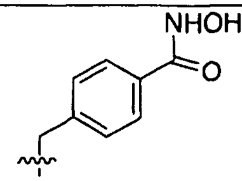
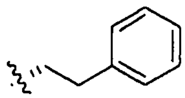
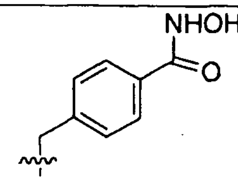
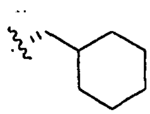
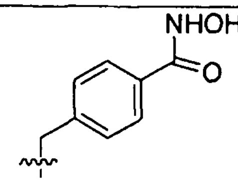
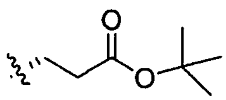
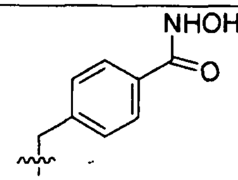
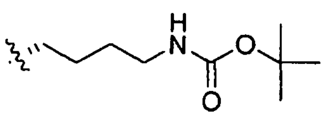
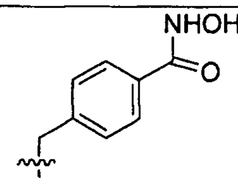
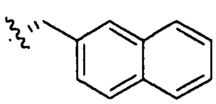
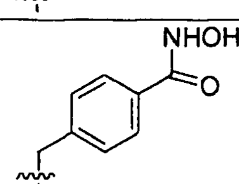
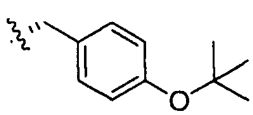
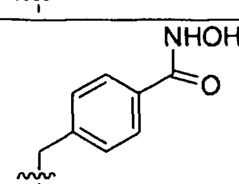
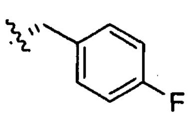
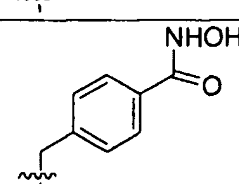
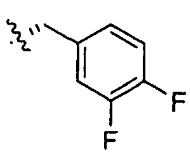
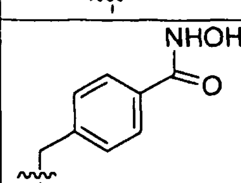
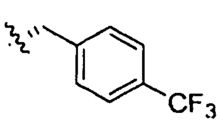
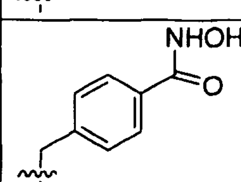
[0045] Another preferred embodiment of Embodiment AA of the present invention, Embodiment CC, provides compounds according to the formula (VII)

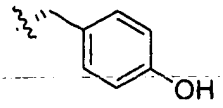
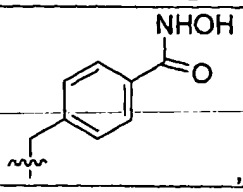
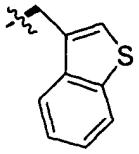
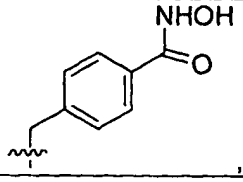
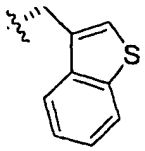
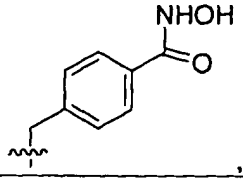
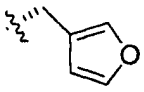
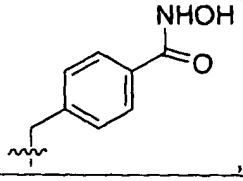
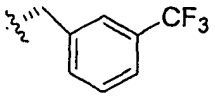
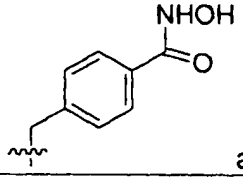
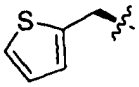
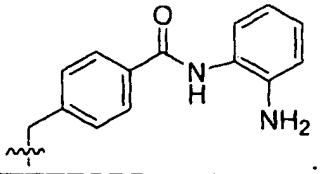


(VII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B, D and E are a combination selected from the group consisting of

D	E	B
	H	
	H	
H		
	H	
H		
H		
	H	

D	E	B
H	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,
	H	 ,

D	E	B
	H	
H		
	H	
	H	
	H	 and
H		

[0046] In another preferred embodiment of Formula (I) of the present invention, Embodiment DD,

n is 0;

X^1, X^2 and X^3 are CH;

X^4 is C-Z;

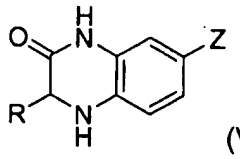
Z is -(C_0-C_7)alkyl-aryl-W;

W is -C(O)-N(R_1)$_2$;

A and B are -H; and

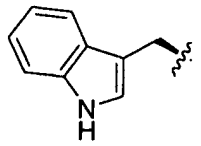
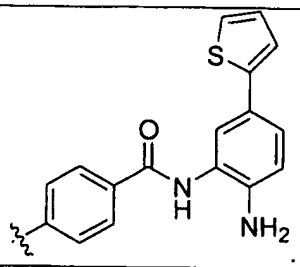
E and D are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-heteroaryl, with the proviso that one of C and D is -H.

[0047] A preferred embodiment of Embodiment DD of the present invention, Embodiment EE, provides compounds according to the formula (VIII)



(VIII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of R and Z is selected from the group consisting of

R	Z
	

[0048] In another preferred embodiment of Formula (I) of the present invention, Embodiment FF,

n is 0;

X^1, X^2 and X^3 are CH;

X^4 is C-Z;

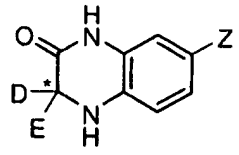
Z is -(C_0-C_7)alkyl-W or -(C_2-C_7)alkenyl-W;

W is -C(O)-NH-OH;

A and B are -H; and

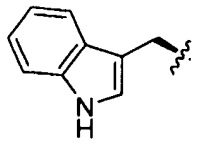
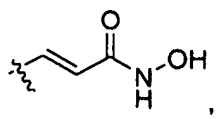
E and D are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-heteroaryl, with the proviso that one of C and D is -H.

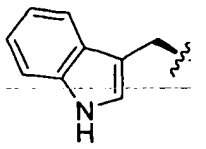
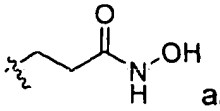
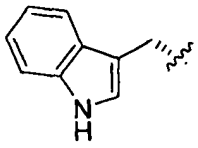
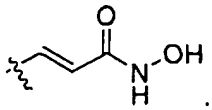
[0049] A preferred embodiment of Embodiment FF of the present invention, Embodiment GG, provides compounds according to the formula (IX)



(IX)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of E, D and Z is selected from the group consisting of

E	D	Z
	H	

E	D	Z
	H	 and
H		

[0050] In another preferred embodiment of Formula (I) of the present invention, Embodiment HH,

n is 1;

X^1 and X^4 are CH;

X^2 and X^3 are C-Z;

Z is selected from the group consisting of -H, -(C_0-C_7)alkyl-W, -(C_0-C_6)alkyl-OR^1, -$N(R^1)$-C(O)-OR^1 and -(C_0-C_3)alkyl-$N(R^1)$-C(O)-(C_1-C_6)alkyl-W;

A is selected from the group consisting of -H and -(C_1-C_7)alkyl-W, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, wherein the aryl and heteoraryl moiety are optionally substituted with one or more substituents selected from the group consisting of R^2;

B is -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl, -(C_1-C_6)alkyl-heteroaryl, -(C_1-C_6)alkyl-W, wherein each of the cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2;

W is independently selected from the group consisting of -C(O)-NH-OH, -C(O)-OR^1, -C(O)-$N(R^1)_2$;

R^1 is independently selected from the group consisting of -H and -(C_0-C_6)-alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_1-C_6)-alkyl wherein each of the aryl and heteroaryl moieties is optionally substituted; and

R^2 is selected from the group consisting of -(C_0-C_6)alkyl substituted with halo, -(C_0-C_6)alkyl-OR_1, -(C_1-C_7)alkyl-W.

[0051] In a preferred embodiment of Embodiment HH of the present invention, Embodiment II,

X^1, X^2, X^3 and X^4 are CH;

A is selected from the group consisting of -(C_1-C_7)alkyl-W;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl, -(C_1-C_6)alkyl-heteroaryl, wherein each of the

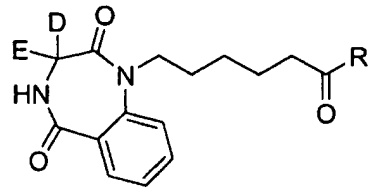
cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2;

W is independently selected from the group consisting of -C(O)-NH-OH, -C(O)-OR^1, -C(O)-$N(R^1)_2$;

R^1 is independently selected from the group consisting of -H, -(C_0-C_6)-alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl, wherein each of the aryl and heteroaryl moieties is optionally substituted; and

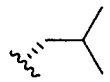
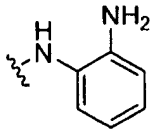
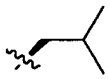
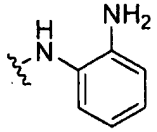
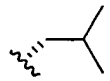
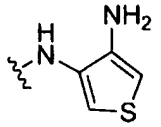
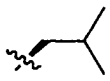
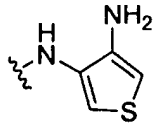
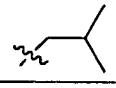
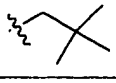
R^2 is selected from the group consisting of -(C_0-C_6)alkyl-OR_1.

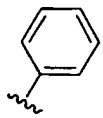
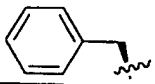
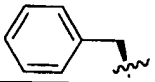
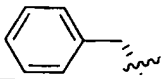
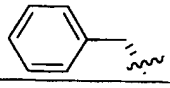
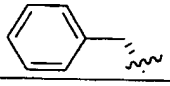
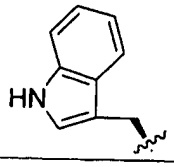
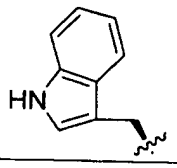
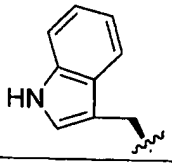
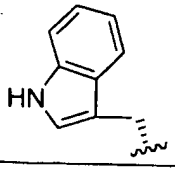
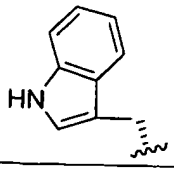
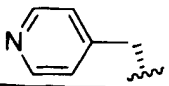
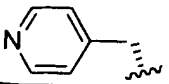
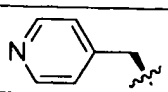
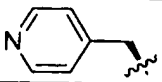
[0052] A preferred embodiment of Embodiment II of the present invention, Embodiment JJ, provides compounds according to the formula (X)

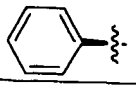
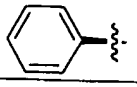
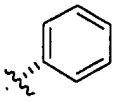
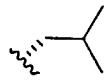
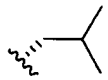
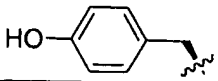
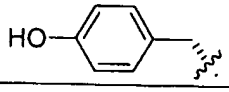
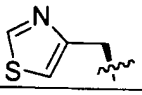
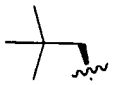
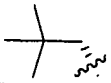
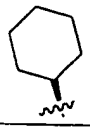
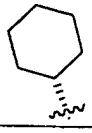
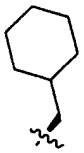
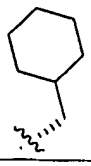


(X)

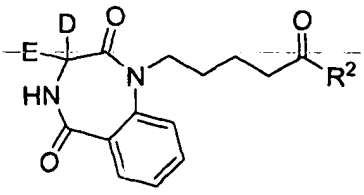
and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein D, E and R are a combination selected from the group consisting of

D	E	R
	H	
H		
	H	
H		
	H	
H	H	
	H	

D	E	R
	H	 ,
H		-OH ,
H		-NH-OH
	H	 ,
	H	-OH ,
	H	-NH-OH ,
H		 ,
H		-OH ,
H		-NH-OH ,
	H	-OH ,
	H	-NH-OH ,
	H	-OH ,
	H	-NH-OH ,
H		-OH ,
H		-NH-OH ,

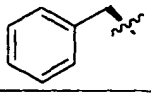
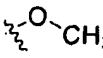
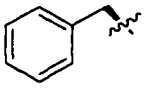
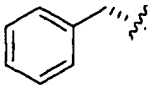
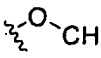
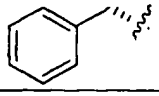
D	E	R
H		-OH ,
H		-NH-OH ,
	H	-NH-OH,
	H	-OH ,
	H	-NH-OH ,
H		-NH-OH,
H		-OH ,
	H	-OH ,
H		-OH ,
		-NH-OH ,
H		-NH-OH ,
	H	-NH-OH ,
H		-NH-OH ,
	H	-NH-OH,
H		-NH-OH ,
	H	-NH-OH ,
H		-NH-OH and
	H	-NH-OH.

[0053] Another preferred embodiment of Embodiment II of the present invention, Embodiment KK, provides compounds according to the formula (XI)



(XI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein D, E and R are a combination selected from the group consisting of

D	E	R
H		 ,
H		-OH,
	H	 and
	H	-OH.

[0054] In another preferred embodiment of Embodiment HH of the present invention, Embodiment LL,

X^1, X^2, X^3 and X^4 are CH;

A is selected from the group consisting of -H, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, wherein the aryl and heteroaryl moiety are optionally substituted with one or more substituents selected from the group consisting of R^2;

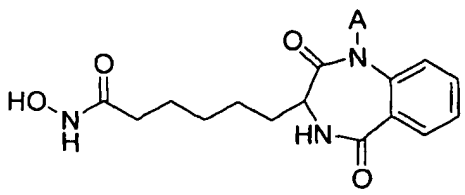
B is -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl-W;

W is -C(O)-NH-OH; and

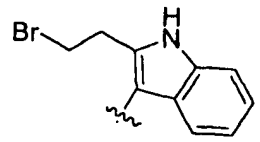
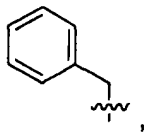
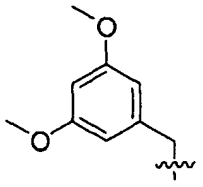
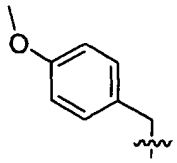
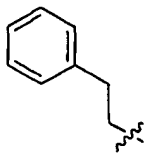
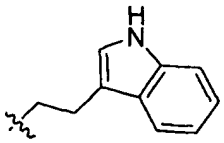
R^2 is selected from the group consisting of -(C_0-C_6)alkyl substituted with halo and -(C_0-C_6)alkyl-OR_1.

[0055] A preferred embodiment of Embodiment LL of the present invention, Embodiment MM, provides compounds according to the formula (XII)



(XII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein A is selected from the group consisting of

	H ,	
		 and
		

[0056] In another preferred embodiment of Embodiment HH of the present invention, Embodiment NN,

X^1, X^2 and X^4 are CH;

X^3 is C-Z;

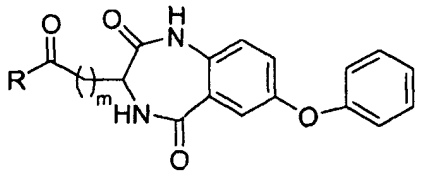
Z is -(C_0-C_6)alkyl-OR^1;

R^1 is -(C_0-C_6)alkyl-aryl;

A is -H;

D and E are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-W; and W is -C(O)-NH-OH and -C(O)-OR^1.

[0057] In a preferred embodiment of Embodiment NN of the present invention, Embodiment OO, provides compounds according to the formula (XIII)



(XIII)

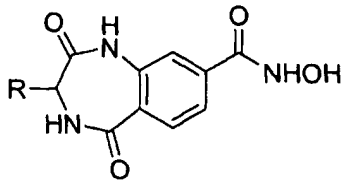
and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of m and R is selected from the group consisting of

m	R,
1	-NH-OH,
2	-NH-OH,
5	-NH-OH,
1	-OH,
2	-OH and
4	-OH.

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl and -(C_1-C_6)alkyl-heteroaryl, wherein each of the cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2; and

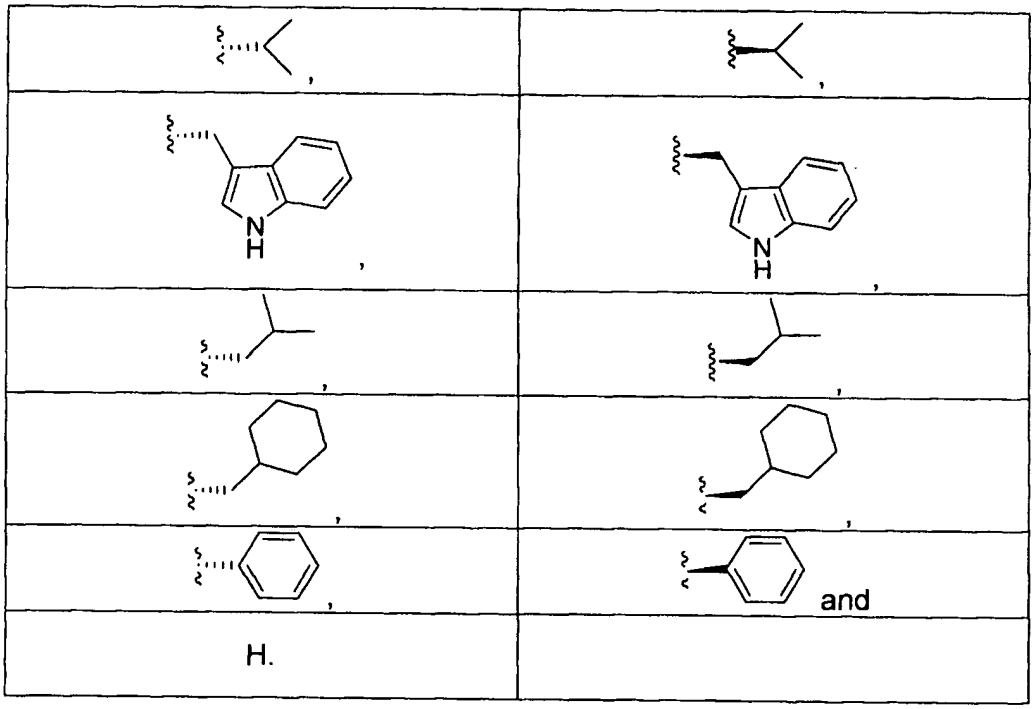
W is -C(O)-NH-OH.

[0061] Another preferred embodiment of Embodiment HH of the present invention, Embodiment SS, provides compounds according to the formula (XV)



(XV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein R is selected from the group consisting of



and

H.

[0062] In another preferred embodiment of the first aspect of the present invention, Embodiment TT, there are provided compounds selected from the group consisting of

Compound No.	Compound
4a	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
4b	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-(2-(methylthio)ethyl)-3-oxoquinoxaline-6-carboxamide,
4c	(S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
4d	(S)-2-sec-butyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
4e	(R)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
4f	(R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,

[0058] In another preferred embodiment of Embodiment HH of the present invention, Embodiment PP,

X^1, X^2 and X^4 are CH;

X^3 is C-Z;

Z is selected from the group consisting of $-N(R^1)-C(O)-OR^1$ and $-(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-W$;

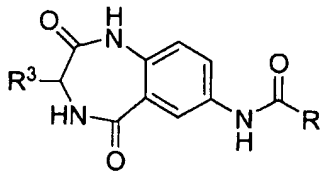
A and B are -H;

D and E are independently selected from the group consisting of -H, $-(C_1-C_6)alkyl$ and $-(C_1-C_6)alkyl-W$;

W is independently selected from the group consisting of -C(O)-NH-OH and $-C(O)-OR^1$; and

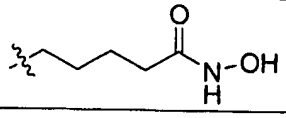
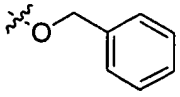
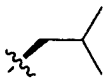
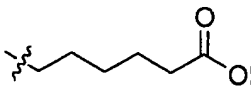
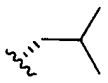
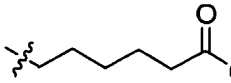
R^1 is independently selected from the group consisting of -H and $-(C_0-C_6)$-alkyl-aryl, wherein the aryl moiety is optionally substituted.

[0059] A preferred embodiment of Embodiment PP of the present invention, Embodiment QQ, provides compounds according to the formula (XIV)



(XIV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of R^3 and R is selected from the group consisting of

R^3	R
	
	 and
	

[0060] In another preferred embodiment of Embodiment HH of the present invention, Embodiment RR,

X^1, X^3 and X^4 are CH;

X^2 is C-Z;

Z is $-(C_0-C_7)alkyl-W$;

A and B are -H;

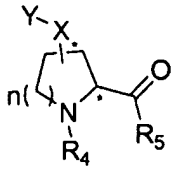
Compound No.	Compound
4g	(S)-1,2,3,4-tetrahydro-N-hydroxy-3-oxo-2-((1-trityl-1H-imidazol-4-yl)methyl)quinoxaline-6-carboxamide,
4h	(S)-2-(4-tert-butoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
4i	(S)-2-Benzyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
4k	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isobutyl-3-oxoquinoxaline-6-carboxamide,
4l	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-((1-methyl-1-H-indol-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide,
5c	(S)-2-((1H-indol-3-yl)methyl)-N-(2-aminophenyl)-1,2,3,4-tetrahydro-3-oxoquinoxaline-6-carboxamide,
6l	(S)-2-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
8	(S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3 oxoquinoxaline-6-carboxamide,
11	(S)-N-(5-(Hydroxycarbamoyl)pentyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
16a	(S)-1-(4-fluorobenzyl)-N-hydroxy-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
16b	(S)-1-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
16c	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-(3-phenylpropyl)quinoxaline-6-carboxamide,
16d	4-(((S)-7-(hydroxycarbamoyl)-2,3-dihydro-3-isopropyl-2-oxoquinoxalin-4(1H)-yl)methyl)benzoic acid,
16e	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-((thiophen-2-yl)methyl)quinoxaline-6-carboxamide,
16f	(S)-N-hydroxy-1-(4-(N-hydroxycarbamimidoyl)benzyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
16g	(S)-1-benzyl-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
16h	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-1-((naphthalen-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide,
18a	(S)-N-hydroxy-2-isopropyl-3-oxo-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
18b	(S)-N-hydroxy-1-(biphenyl-4-sulfonyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
18c	(S)-N-hydroxy-2-isopropyl-3-oxo-1-(2,4,6-trimethybenzenesulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
18e	(S)-N-hydroxy-1-(4-methoxybenzenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
18f	(S)-N-hydroxy-1-(1-naphthalenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
23a	N1-(2-Aminophenyl)-N8-((S)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)octanediamide,
24a	N1-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
24e	N1-((R)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
24f	N1-((R)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
26e	N1-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
29a	N-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-8-(oxazol-2-yl)-8-

Compound No.	Compound
	oxooctanamide,
43	6-((R)-1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxy-4-oxy-hexanamide,
47a	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxyhexanamide,
47b	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-aminophenyl)hexanamide,
49	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)hexanamide,
$54a_1$	4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
$54a_2$	4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
$54b_1$	N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-benzamide,
$54b_2$	(R)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_3$	(S)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_4$	(S)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_5$	(R)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_6$	N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
$54b_7$	(R)-N-hydroxy-4-((3-oxo-2-phenethyl-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
$54b_8$	(R)-4-((2-(cyclohexylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_9$	(R)-tert-butyl 4-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)butylcarbamate,
$54b_{10}$	(R)-N-hydroxy-4-((2-(naphthalen-2-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
$54b_{11}$	(R)-4-((2-(4-tert-butoxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{12}$	(R)-tert-butyl 3-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)propanoate,
$54b_{13}$	(R)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{14}$	(S)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{15}$	(R)-4-((2-(4-fluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{16}$	(R)-4-((2-(3,4-difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{17}$	(R)-4-((2-(4-trifluoromethylbenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{18}$	(R)-N-hydroxy-4-((2-(4-hydroxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
$54b_{19}$	(R)-N-hydroxy-4-((2-(3-(trifluoromethyl)benzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
$54b_{20}$	(R)-4-((2-(furan-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
$54b_{21}$	(R)-N-hydroxy-4-((3-oxo-2-(pyridin-3-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,

Compound No.	Compound
54c	(S)-N-(2-aminophenyl)-4-((3-oxo-2-(thiophen-2-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
56a	4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
62	4-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)benzamide,
66c	(E)-3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide,
66f	(E)-3-((R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide,
$68b_1$	6-((S)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_3$	6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_4$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_6$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_7$	6-((S)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_8$	6-((R)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_9$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{11}$	6-((S)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{12}$	6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{16}$	6-(3,3-spirocyclopentyl-2,5-dioxo-2,3,4,5,tetrahydrobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{17}$	6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{18}$	6-((R)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{19}$	6-((S)-3-cyclohexyl-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{20}$	6-((S)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{21}$	6-((R)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{22}$	6-((S)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
$68b_{23}$	6-((R)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
69	3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxypropanamide,
71	N-(2-aminophenyl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide,
72	N-(4-aminothiophen-3-yl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide,
74	6-(2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
79	6-(1-(2-(1H-indol-3-yl)ethyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-

Compound No.	Compound
	benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
80	6-(1-benzyl-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
81	6-(1-(3,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
82	6-(1-(4-methoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
83	6-(2,3,4,5-tetrahydro-2,5-dioxo-1-phenethyl-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
88a	6-(2,3,4,5-tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
92a	6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
92b	(S)-benzyl 3-(6-(hydroxyamino)-6-oxohexyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-7-ylcarbamate,
97a	(R)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97b	(S)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97c	(S)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97d	(R)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97f	(R)-N-hydroxy-3-isobutyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97g	(R)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97h	(S)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97i	(S)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
97j	(R)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide and
97k	N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide.

[0063] In the second aspect of the present invention there is provided compounds of formula (XVI),



(XVI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein

n is 1 or 2;

X is selected from the group consisting of -O-, -S-, -N(R^1)- and -CH(R^1)-;

Y is selected from the group consisting of -(C_0-C_7)alkyl-heteroaryl-W, -(C_1-C_7)alkyl-W, -(C_0-C_7)alkyl-aryl-W and -C(O)-(C_1-C_7)alkyl-W;

with the proviso that when X is $N(R^1)$, Y is $-C(O)-(C_1-C_7)$alkyl-W or $-S(O)_2-(C_1-C_6)$alkyl-W.

[0064] In a preferred embodiment of Formula (XV) of the present invention, Embodiment UU, Q is selected from the group consisting of thiopheneyl, furanyl, tetrazolyl, imidazolyl, pyridinyl and pyrimidinyl.

[0065] In another preferred embodiment of Formula (XV) of the present invention, Embodiment VV,

n is 1;

X is -O-;

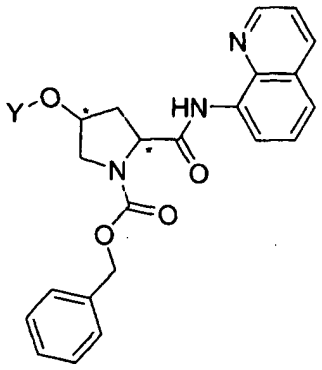
Y is selected from the group consisting of $-(C_1-C_7)$alkyl-W, $-(C_0-C_7)$alkyl-aryl-W and $-C(O)-(C_1-C_7)$alkyl-W;

W is -C(O)-NH-OH;

R^4 is $-C(O)-OR^1$; and

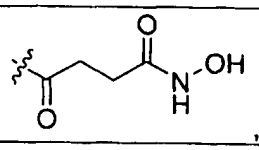
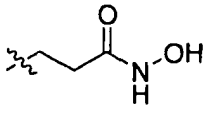
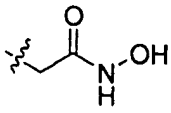
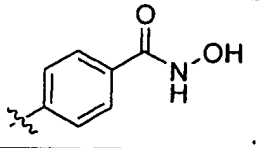
R^5 is $-N(R^1)_2$.

[0066] A preferred embodiment of Embodiment VV of the present invention, Embodiment WW, provides compounds according to the formula XVII



(XVII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein Y is selected from the group consisting of

		 and
		

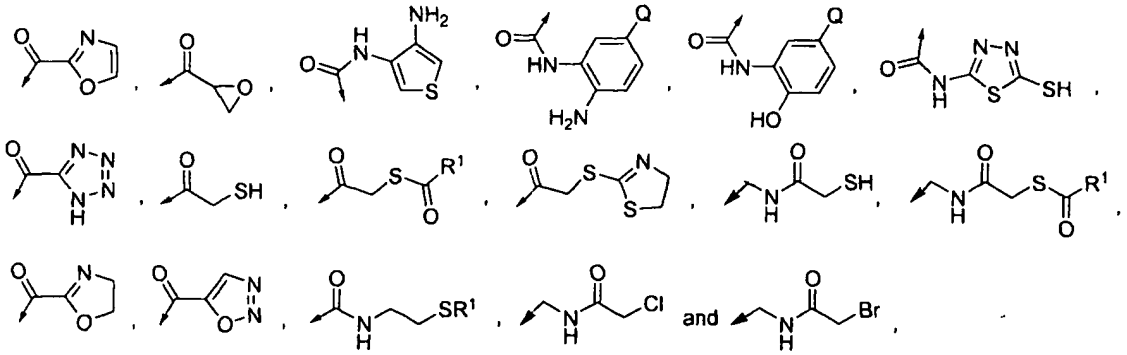
[0067] Another preferred embodiment of the second aspect of the present invention, Embodiment XX, provides compounds selected from the group consisting of

Cpd No.	Compound
109a	(2S,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
109b	(2S,4R)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-(C_1-C_4)alkyl, -C(O)-N(R^1)$_2$, -(C_2-C_6)alkyl-N(OH)-C(O)H-, -(C_1-C_6)alkyl-SR^1, -(C_1-C_6)alkyl-SC(O)-(C_1-C_4)alkyl, -C(O)-OR^1, -C(O)-(C_1-C_4)alkylepoxide, -C(O)-(C_1-C_4)alkyl-SH, -C(O)-(C_1-C_4)alkyl-SC(O)R^1, -C(O)-(C_1-C_4)alkyl-S-heteroaryl, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-halo, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SH, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SC(O)R^1, -C(O)-NH-(C_2-C_6)alkyl-SH and -C(O)-(C_1-C_6)alkyl,

wherein the alkyl of said -C(O)-(C_1-C_6)alkyl is optionally substituted with one or more substituents selected from the group consisting of mono to per-halogenated -(C_1-C_6)alkyl, -C(O)-heteroaryl, -C(O)-NH-heteroaryl and -C(O)-NH-aryl;

wherein each aryl and heteroaryl is optionally substituted with one or more substituents selected from the group consisting of -NH_2, -OH, SH, -CN, -NO_2, -N(R^1)$_2$, halo, mono- to per-halogenated-(C_1-C_6)alkyl, aryl, heteroaryl,



wherein Q is selected from the group consisting of heterocyclic, aryl and heteroaryl;

R^1 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_8)cycloalkyl, -heterocyclyl, -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl,

wherein each afore-mentioned R^1 aryl, heteroaryl, cycloalkyl and heterocyclyl moiety is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, -SH, mono- to per-halogenated-(C_1-C_6)alkyl and -(C_2-C_4)alkyl-N(R^1)$_2$,

wherein optionally the R^1 together with the nitrogen atom to which they are attached form a heterocyclyl group;

R^4 is selected from the group consisting of -S(O)$_2$-(C_1-C_6)alkyl, -S(O)$_2$-(C_1-C_6)heteroalkyl, -S(O)$_2$-(C_1-C_6)aryl, -S(O)$_2$-(C_1-C_6)alkylaryl, -S(O)$_2$-(C_1-C_6)heteroaryl, -S(O)$_2$-(C_1-C_6)arylalkyl, -S(O)$_2$-(C_1-C_6)heterocyclic, -C(O)-(C_1-C_6)alkyl, -C(O)-(C_1-C_6)heteroalkyl, -C(O)-(C_1-C_6)aryl, -C(O)-(C_1-C_6)alkylaryl, -C(O)-(C_1-C_6)heteroaryl, -C(O)-(C_1-C_6)arylalkyl, -C(O)-(C_1-C_6)heterocyclic and -C(O)-OR^1;

R^5 is selected from the group consisting of -OR^1 and -N(R^1)$_2$; and

the asterick mark * indicates a chiral carbon atom,

Cpd No.	Compound
109c	(2R,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
112a	(2S,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
112b	(2S,4R)-benzyl 4-(2-(hydroxyamino)-2-oxoethoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate and
112c	(2R,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate.

[0068] In another preferred embodiment of Formula (I) of the present invention

X^1, X^2, X^3 and X^4 are absent;

X^5 is a covalent bond;

X^6 is CH_2;

n is 1;

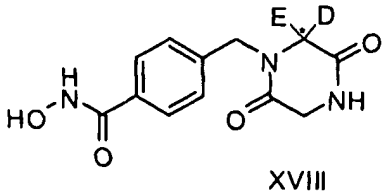
B is -$(C_0$-$C_7)$alkyl-aryl-$(C_0$-$C_4)$alkyl-W;

W is -C(O)NHOH;

A is H; and

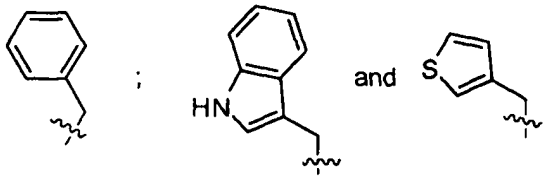
E and D are independently selected from a group consisting of -H, -$(C_0$-$C_6)$alkyl-aryl- and -$(C_0$-$C_6)$alkyl-heteroaryl-, wherein each aryl and heteroaryl moiety is optionally substituted with one or more R^2. Preferably, E and D are independently selected from the group consisting of -H, -$(C_1$-$C_6)$alkyl-aryl- and -$(C_1$-$C_6)$alkyl-heteroaryl-.

[0069] Another preferred embodiment of Formula (I) of the present invention provides compounds according to Formula (XVIII)



XVIII

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof. In a preferred embodiment, one of D and E is H and the other is selected from the group consisting of



, wherein each aryl and heteroaryl moeity is optionally substituted with one or more groups selected from R^2.

[0070] In another preferred embodiment of Formula (I), only one of Z, A, B, D and E end in with the moiety W.

[0071] In the third aspect of the present invention, the invention provides a composition comprising a compound according to the first aspect or second aspects or Embodiments A

to XX, and a pharmaceutically acceptable carrier, diluent or excipient. In one embodiment, the composition comprises a compound according to the first aspect or second aspects or Embodiments A to XX, together with an additional HDAC inhibitor known in the art or which will be discovered, and a pharmaceutically acceptable carrier, diluent or excipient. In a preferred embodiment, the additional HDAC inhibitor is a small molecule or a nucleic acid level inhibitor of histone deacetylase.

[0072] In the fourth aspect, the invention provides a method of inhibiting histone deacetylase. In one embodiment, the method comprises contacting the histone deacetylase with an inhibiting effective amount of a compound according to the first aspect or second aspect or Embodiments A to XX. In a further embodiment of the fourth aspect, the method comprises contacting the histone deacetylase with an inhibiting effective amount of a composition according to the third aspect. In still another embodiment, the method of inhibiting histone deacetylase further comprises contacting the histone deacetylase with an additional HDAC inhibitor known in the art or which will be discovered in an amount sufficient to inhibit histone decetylase. In a preferred embodiment, the HDAC inhibitors act synergistically to inhibit histone deacetylase. In yet another embodiment, the invention provides a method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with an inhibiting effective amount of compound according to the first aspect or the second aspect or Embodiments A to XX. In still another embodiment, the method of inhibiting histone deacetylase in a cell comprises contacting the cell with an inhibiting effective amount of a composition according to the third aspect. In still another embodiment, the method of inhibiting histone deacetylase in a cell further comprises contacting the cell with an additional HDAC inhibitor known in the art or which will be discovered and/or a nucleic acid level inhibitor of histone deacetylase in an amount sufficient to inhibit histone decetylase. In a preferred embodiment, the HDAC inhibitors act synergistically to inhibit histone deacetylase activity.

[0073] For purposes of the present invention, the following definitions will be used (unless expressly stated otherwise):

[0074] As used herein, the terms "histone deacetylase" and "HDAC" are intended to refer to any one of a family of enzymes that remove acetyl groups from the ε-amino groups of lysine residues at the *N*-terminus of a histone. Unless otherwise indicated by context, the term "histone" is meant to refer to any histone protein, including H1, H2A, H2B, H3, H4, and H5, from any species. Preferred histone deacetylases include class I and class II enzymes. Other preferred histone deacetylases include class III enzymes. Preferably the histone deacetylase is a human HDAC, including, but not limited to, HDAC-1, HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7, HDAC-8, HDAC-9, HDAC-10, HDAC-11, SirT1, SirT2,

SirT3, SirT4, SirT5, SirT6 and SirT7. In some other preferred embodiments, the histone deacetylase is derived from a plant, protozoal or fungal source.

[0075] The terms "histone deacetylase inhibitor" and "inhibitor of histone deacetylase" are intended to mean a compound having a structure as defined herein, which is capable of interacting with a histone deacetylase and inhibiting its enzymatic activity.

[0076] The term "inhibiting histone deacetylase enzymatic activity" is intended to mean reducing the ability of a histone deacetylase to remove an acetyl group from a histone. The concentration of inhibitor which reduces the activity of a histone deacetylase to 50% of that of the uninhibited enzyme is determined as the IC_{50} value.

[0077] The term "inhibiting effective amount" is meant to denote a dosage sufficient to cause inhibition of histone deacetylase activity. The histone deacetylase can be in a cell, which cell can be in a multicellular organism. The multicellular organism can be, for example, a plant, a fungus or an animal, preferably a mammal and more preferably a human. If in a multicellular organism, the method according to this aspect of the invention comprises administering to the organism a compound or composition according to the present invention. Administration may be by any route, including, without limitation, parenteral, oral, sublingual, transdermal, topical, intranasal, intratracheal, or intrarectal. In certain particularly preferred embodiments, compounds of the invention are administered intravenously in a hospital setting. In certain other preferred embodiments, administration may preferably be by the oral route.

[0078] Preferably, such inhibition is specific, *i.e.*, the histone deacetylase inhibitor reduces the ability of a histone deacetylase to remove an acetyl group from a histone at a concentration that is lower than the concentration of the inhibitor that is required to produce another, unrelated biological effect. Preferably, the concentration of the inhibitor required for histone deacetylase inhibitory activity is at least 2-fold lower, more preferably at least 5-fold lower, even more preferably at least 10-fold lower, and most preferably at least 20-fold lower than the concentration required to produce an unrelated biological effect.

[0079] For simplicity, chemical moieties are defined and referred to throughout primarily as univalent chemical moieties (*e.g.*, alkyl, aryl, etc.). Nevertheless, such terms are also used to convey corresponding multivalent moieties under the appropriate structural circumstances clear to those skilled in the art. For example, while an "alkyl" moiety generally refers to a monovalent radical (*e.g.* CH_3-CH_2-), in certain circumstances a bivalent linking moiety can be "alkyl," in which case those skilled in the art will understand the alkyl to be a divalent radical (*e.g.*, -CH_2-CH_2-), which is equivalent to the term "alkylene." (Similarly, in circumstances in which a divalent moiety is required and is stated as being "aryl," those skilled in the art will understand that the term "aryl" refers to the corresponding divalent

moiety, arylene). All atoms are understood to have their normal number of valences for bond formation (*i.e.*, 4 for carbon, 3 for N, 2 for O, and 2, 4, or 6 for S, depending on the oxidation state of the S). On occasion a moiety may be defined, for example, as $(A)_a$-B-, wherein a is 0 or 1. In such instances, when a is 0 the moiety is B- and when a is 1 the moiety is A-B-.

[0080] For simplicity, reference to a "C_n-C_m" heterocyclyl or "C_n-C_m" heteroaryl means a heterocyclyl or heteroaryl having from "n" to "m" annular atoms, where "n" and "m" are integers. Thus, for example, a C_5-C_6-heterocyclyl is a 5- or 6- membered ring having at least one heteroatom, and includes pyrrolidinyl (C_5) and piperidinyl (C_6); C_6-heteroaryl includes, for example, pyridyl and pyrimidyl.

[0081] The term "hydrocarbyl" refers to a straight, branched, or cyclic alkyl, alkenyl, or alkynyl, each as defined herein. A "C_0" hydrocarbyl is used to refer to a covalent bond. Thus, "C_0-C_3-hydrocarbyl" includes a covalent bond, methyl, ethyl, ethenyl, ethynyl, propyl, propenyl, propynyl, and cyclopropyl.

[0082] The term "alkyl" is intended to mean a straight or branched chain aliphatic group having from 1 to 12 carbon atoms, preferably 1-8 carbon atoms, and more preferably 1-6 carbon atoms, which is optionally substituted with one, two or three substituents. Other preferred alkyl groups have from 2 to 12 carbon atoms, preferably 2-8 carbon atoms and more preferably 2-6 carbon atoms. Preferred alkyl groups include, without limitation, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, and hexyl. A "C_0" alkyl (as in "C_0-C_3-alkyl") is a covalent bond.

[0083] The term "alkenyl" is intended to mean an unsaturated straight or branched chain aliphatic group with one or more carbon-carbon double bonds, having from 2 to 12 carbon atoms, preferably 2-8 carbon atoms, and more preferably 2-6 carbon atoms, which is optionally substituted with one, two or three substituents. Preferred alkenyl groups include, without limitation, ethenyl, propenyl, butenyl, pentenyl, and hexenyl.

[0084] The term "alkynyl" is intended to mean an unsaturated straight or branched chain aliphatic group with one or more carbon-carbon triple bonds, having from 2 to 12 carbon atoms, preferably 2-8 carbon atoms, and more preferably 2-6 carbon atoms, which is optionally substituted with one, two or three substituents. Preferred alkynyl groups include, without limitation, ethynyl, propynyl, butynyl, pentynyl, and hexynyl.

[0085] The terms "alkylene," "alkenylene," or "alkynylene" as used herein are intended to mean an alkyl, alkenyl, or alkynyl group, respectively, as defined hereinabove, that is positioned between and serves to connect two other chemical groups. Preferred alkylene groups include, without limitation, methylene, ethylene, propylene, and butylene. Preferred alkenylene groups include, without limitation, ethenylene, propenylene, and butenylene.

Preferred alkynylene groups include, without limitation, ethynylene, propynylene, and butynylene.

[0086] The term "cycloalkyl" is intended to mean a saturated or unsaturated cyclic hydrocarbon group having 3 to 12 carbons, preferably 3 to 8 carbons, and more preferably 3 to 6 carbons, wherein the cycloalkyl group additionally is optionally substituted. Preferred cycloalkyl groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cyclooctyl.

[0087] The term "heteroalkyl" is intended to mean a saturated or unsaturated, straight or branched chain aliphatic group, wherein one or more carbon atoms in the chain are independently replaced by a heteroatom selected from the group consisting of O, S, and N.

[0088] The term "aryl" is intended to mean a C_6-C_{14} aromatic moiety comprising one to three aromatic rings, which is optionally substituted. Preferably, the aryl group is a C_6-C_{10} aryl group, more preferably a C_6 aryl group. Preferred aryl groups include, without limitation, phenyl, naphthyl, anthracenyl, and fluorenyl.

[0089] The terms "aralkyl" or "arylalkyl" is intended to mean a group comprising an aryl group covalently linked to an alkyl group, either of which may independently be optionally substituted or unsubstituted. Preferably, the aralkyl group is (C_1-C_6)alk(C_6-C_{10})aryl, including, without limitation, benzyl, phenethyl, and naphthylmethyl. For simplicity, when written as "arylalkyl" this term, and terms related thereto, is intended to indicate the order of groups in a compound as "aryl – alkyl". Similarly, "alkyl-aryl" is intended to indicate the order of the groups in a compound as "alkyl-aryl".

[0090] The terms "heterocyclyl", "heterocyclic" or "heterocycle" are intended to mean a group which is an optionally substituted aromatic or, preferably, non-aromatic mono-, bi-, or tricyclic structure having from about 3 to about 14 atoms, wherein one or more atoms are independently selected from the group consisting of N, O, and S. One ring of a bicyclic heterocycle or one or two rings of a tricyclic heterocycle may be aromatic, as in indan and 9,10-dihydro anthracene. The heterocyclic group is optionally substituted on carbon with, for example, oxo or with one of the substituents listed above. The heterocyclic group may also independently be substituted on nitrogen with, for example, alkyl, aryl, aralkyl, alkylcarbonyl, alkylsulfonyl, arylcarbonyl, arylsulfonyl, alkoxycarbonyl, aralkoxycarbonyl, or on sulfur with oxo or lower alkyl. Preferred heterocyclic groups include, without limitation, epoxy, aziridinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, thiazolidinyl, oxazolidinyl, oxazolidinonyl, and morpholino. In certain preferred embodiments, the heterocyclic group is fused to an aryl, heteroaryl, or cycloalkyl group. Examples of such fused heterocycles include, without limitation, tetrahydroquinoline and dihydrobenzofuran. Specifically excluded

from the scope of this term are compounds where an annular O or S atom is adjacent to another O or S atom.

[0091] In certain preferred embodiments, the heterocyclic group is a heteroaryl group. As used herein, the term "heteroaryl" is intended to mean an optionally substituted group having 5 to 14 ring atoms, preferably 5, 6, 9, or 10 ring atoms; having 6, 10, or 14 pi electrons shared in a cyclic array; and having, in addition to carbon atoms, between one or more heteroatoms independently selected from the group consisting of N, O, and S. For example, a heteroaryl group may be pyrimidinyl, pyridinyl, benzimidazolyl, thienyl, benzothiazolyl, benzofuranyl and indolinyl. Preferred heteroaryl groups include, without limitation, thienyl, benzothienyl, furyl, benzofuryl, dibenzofuryl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indolyl, quinolyl, isoquinolyl, quinoxalinyl, tetrazolyl, oxazolyl, thiazolyl, and isoxazolyl.

[0092] The terms "arylene," "heteroarylene," or "heterocyclylene" are intended to mean an aryl, heteroaryl, or heterocyclyl group, respectively, as defined hereinabove, that is positioned between and serves to connect two other chemical groups.

[0093] Preferred heterocyclyls and heteroaryls include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4aH-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, and xanthenyl.

[0094] As employed herein, when a moiety (*e.g.*, alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, etc.) is described as "optionally substituted" it is meant that the

group optionally has from one to four, preferably from one to three, more preferably one or two, non-hydrogen substituents. Suitable substituents include, without limitation, halo, hydroxy, oxo (*e.g.*, an annular -CH- substituted with oxo is -C(O)-) nitro, halohydrocarbyl, hydrocarbyl, aryl, aralkyl, alkoxy, aryloxy, amino, acylamino, alkylcarbamoyl, arylcarbamoyl, aminoalkyl, acyl, carboxy, hydroxyalkyl, alkanesulfonyl, arenesulfonyl, alkanesulfonamido, arenesulfonamido, aralkylsulfonamido, alkylcarbonyl, acyloxy, cyano, and ureido groups. Preferred substituents, which are themselves not further substituted (unless expressly stated otherwise) are:

(a) halo, cyano, oxo, carboxy, formyl, nitro, amino, amidino, guanidino,

(b) C_1-C_5 alkyl or alkenyl or arylalkyl imino, carbamoyl, azido, carboxamido, mercapto, hydroxy, hydroxyalkyl, alkylaryl, arylalkyl, C_1-C_8 alkyl, C_1-C_8 alkenyl, C_1-C_8 alkoxy, C_1-C_8 alkoxycarbonyl, aryloxycarbonyl, C_2-C_8 acyl, C_2-C_8 acylamino, C_1-C_8 alkylthio, arylalkylthio, arylthio, C_1-C_8 alkylsulfinyl, arylalkylsulfinyl, arylsulfinyl, C_1-C_8 alkylsulfonyl, arylalkylsulfonyl, arylsulfonyl, C_0-C_6 *N*-alkyl carbamoyl, C_2-C_{15} *N,N*-dialkylcarbamoyl, C_3-C_7 cycloalkyl, aroyl, aryloxy, arylalkyl ether, aryl, aryl fused to a cycloalkyl or heterocycle or another aryl ring, C_3-C_7 heterocycle, C_5-C_{15} heteroaryl or any of these rings fused or spiro-fused to a cycloalkyl, heterocyclyl, or aryl, wherein each of the foregoing is further optionally substituted with one more moieties listed in (a), above; and

(c) $-(CH_2)_n-NR_{30}R_{31}$, wherein n is from 0 (in which case the nitrogen is directly bonded to the moiety that is substituted) to 6, and R_{30} and R_{31} are each independently hydrogen, cyano, oxo, carboxamido, amidino, C_1-C_8 hydroxyalkyl, C_1-C_3 alkylaryl, aryl-C_1-C_3 alkyl, C_1-C_8 alkyl, C_1-C_8 alkenyl, C_1-C_8 alkoxy, C_1-C_8 alkoxycarbonyl, aryloxycarbonyl, aryl-C_1-C_3 alkoxycarbonyl, C_2-C_8 acyl, C_1-C_8 alkylsulfonyl, arylalkylsulfonyl, arylsulfonyl, aroyl, aryl, cycloalkyl, heterocyclyl, or heteroaryl, wherein each of the foregoing is further optionally substituted with one more moieties listed in (a), above; or

R^{30} and R^{31} taken together with the N to which they are attached form a heterocyclyl or heteroaryl, each of which is optionally substituted with from 1 to 3 substituents from (a), above.

[0095] A "halohydrocarbyl" is a hydrocarbyl moiety in which from one to all hydrogens have been replaced with one or more halo.

[0096] The term "halogen" or "halo" is intended to mean chlorine, bromine, fluorine, or iodine. As herein employed, the term "acyl" refers to an alkylcarbonyl or arylcarbonyl moiety. The term "acylamino" refers to an amide group attached at the nitrogen atom (*i.e.*, R-CO-NH-). The term "carbamoyl" refers to an amide group attached at the carbonyl carbon atom (*i.e.*, NH_2-CO-). The nitrogen atom of an acylamino or carbamoyl substituent is

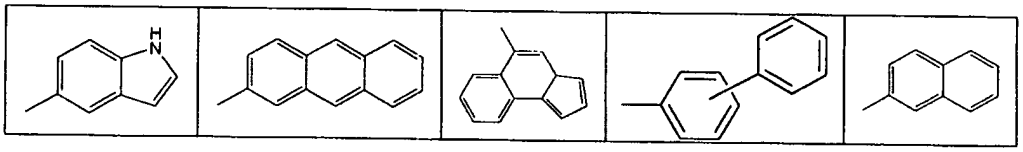
additionally optionally substituted. The term "sulfonamido" refers to a sulfonamide substituent attached by either the sulfur or the nitrogen atom. The term "amino" is meant to include NH_2, alkylamino, arylamino, and cyclic amino groups. The term "ureido" as employed herein refers to a substituted or unsubstituted urea moiety.

[0097] The term "radical" is intended to mean a chemical moiety comprising one or more unpaired electrons.

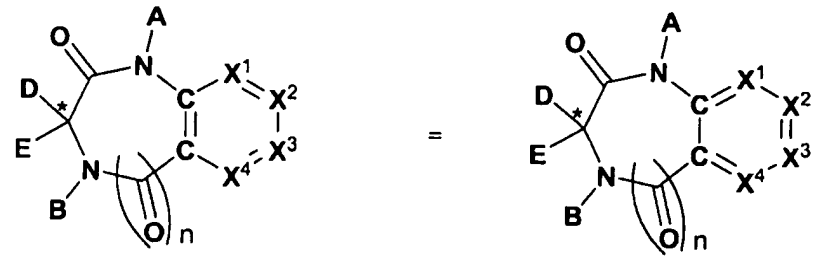
[0098] A moiety that is substituted is one in which one or more hydrogens have been independently replaced with another chemical substituent. As a non-limiting example, substituted phenyls include 2-flurophenyl, 3,4-dichlorophenyl, 3-chloro-4-fluoro-phenyl, 2-fluoro-3-propylphenyl. As another non-limiting example, substituted *N*-octyls include 2,4-dimethyl-5-ethyl-octyl and 3-cyclopentyl-octyl. Included within this definition are methylenes ($-CH_2-$) substituted with oxygen to form carbonyl -CO-).

[0099] Where optional substituents are chosen from "one or more" groups it is to be understood that this definition includes all substituents being chosen from one of the specified groups or the substituents being chosen from two or more of the specified groups.

[0100] In addition, substituents on cyclic moieties (i.e., cycloalkyl, heterocyclyl, aryl, heteroaryl) include 5-6 membered mono- and 9-14 membered bi-cyclic moieties fused to the parent cyclic moiety to form a bi- or tri-cyclic fused ring system. Substituents on cyclic moieties also include 5-6 membered mono- and 9-14 membered bi-cyclic moieties attached to the parent cyclic moiety by a covalent bond to form a bi- or tri-cyclic bi-ring system. For example, an optionally substituted phenyl includes, but is not limited to, the following:



[0101] As will be understood by those skilled in the art, when X^5 and X^6 together are -C=C-, different, but equivalent resonance structures may be drawn, as in, for example:



[0102] An "unsubstituted" moiety as defined above (*e.g.*, unsubstituted cycloalkyl, unsubstituted heteroaryl, etc.) means that moiety as defined above that does not have any of the optional substituents for which the definition of the moiety (above) otherwise provides.

Thus, for example, while an "aryl" includes phenyl and phenyl substituted with a halo, "unsubstituted aryl" does not include phenyl substituted with a halo.

[0103] Some compounds of the invention may have chiral centers and/or geometric isomeric centers (E- and Z- isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomers and geometric isomers. The invention also comprises all tautomeric forms of the compounds disclosed herein.

[0104] The present invention also includes prodrugs of compounds of the invention. The term "prodrug" is intended to represent covalently bonded carriers, which are capable of releasing the active ingredient of the prodrug when the prodrug is administered to a mammalian subject. Release of the active ingredient occurs *in vivo*. Prodrugs can be prepared by techniques known to one skilled in the art. These techniques generally modify appropriate functional groups in a given compound. These modified functional groups however regenerate original functional groups by routine manipulation or *in vivo*. Prodrugs of compounds of the present invention include compounds wherein a hydroxy, amino, carboxylic, or a similar group is modified. Examples of prodrugs include, but are not limited to esters (e.g., acetate, formate, and benzoate derivatives), carbamates (e.g., N,N-dimethylaminocarbonyl) of hydroxy or amino functional groups in compounds of the invention, amides (e.g., trifluoroacetylamino, acetylamino, and the like), and the like.

[0105] The compounds of the invention may be administered as is or in the form of an *in vivo* hydrolyzable ester or *in vivo* hydrolyzable amide. An *in vivo* hydrolyzable ester of a compound of the invention containing carboxy or hydroxy group is, for example, a pharmaceutically acceptable ester which is hydrolyzed in the human or animal body to produce the parent acid or alcohol. Suitable pharmaceutically acceptable esters for carboxy include C_{1-6}-alkoxymethyl esters (*e.g.*, methoxymethyl), C_{1-6}-alkanoyloxymethyl esters (*e.g.*, for example pivaloyloxymethyl), phthalidyl esters, C_{3-8}-cycloalkoxycarbonyloxyC_{1-6}-alkyl esters (*e.g.*, 1-cyclohexylcarbonyloxyethyl); 1,3-dioxolen-2-onylmethyl esters (*e.g.*, 5-methyl-1,3-dioxolen-2-onylmethyl; and C_{1-6}-alkoxycarbonyloxyethyl esters (*e.g.*, 1-methoxycarbonyloxyethyl) and may be formed at any carboxy group in the compounds of this invention.

[0106] An *in vivo* hydrolyzable ester of a compound of the invention containing a hydroxy group includes inorganic esters such as phosphate esters and a-acyloxyalkyl ethers and related compounds which as a result of the in vivo hydrolysis of the ester breakdown to give the parent hydroxy group. Examples of α-acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxy-methoxy. A selection of *in vivo* hydrolyzable ester forming groups for hydroxy include alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, alkoxycarbonyl (to give alkyl carbonate esters), dialkylcarbamoyl and *N*-(*N*,*N*-

dialkylaminoethyl)-*N*-alkylcarbamoyl (to give carbamates), *N,N*-dialkylaminoacetyl and carboxyacetyl. Examples of substituents on benzoyl include morpholino and piperazino linked from a ring nitrogen atom via a methylene group to the 3- or 4- position of the benzoyl ring. A suitable value for an *in vivo* hydrolyzable amide of a compound of the invention containing a carboxy group is, for example, a *N*-C_{1-6}-alkyl or N,N-di-C_{1-6}-alkyl amide such as *N*-methyl, *N*-ethyl, *N*-propyl, *N,N*-dimethyl, *N*-ethyl-*N*-methyl or *N,N*-diethyl amide.

[0107] The foregoing merely summarizes the various aspects and preferred embodiments thereof, of the invention and is not intended to be limiting in nature. These aspects and embodiments are described more fully below.

Compounds

[0108] The data presented herein demonstrate the histone deacetylase inhibitory effects of the compounds of the invention. These data lead one to reasonably expect that the compounds of the invention are useful for inhibition of histone deacetylase.

[0109] Preferred compounds according to the invention include those in the Table 1, which were prepared essentially using the methods described herein and illustrated below in the Schemes. These examples merely serve to exemplify some of the compounds of the first and second aspects of the invention and do not limit the scope of the invention. All of the compounds in this application were named using Chemdraw Ultra version 10.0, which is available through Cambridgesoft.co, 100 Cambridge Park Drive, Cambridge, MA 02140, Namepro version 5.09, which is available from ACD labs, 90 Adelaide Street West, Toronto, Ontario, M5H, 3V9, Canada, or were derived therefrom.

Table 1

Cpd No.	Compound
4a	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide
4b	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-(2-(methylthio)ethyl)-3-oxoquinoxaline-6-carboxamide
4c	(S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
4d	(S)-2-sec-butyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
4e	(R)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide
4f	(R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
4g	(S)-1,2,3,4-tetrahydro-N-hydroxy-3-oxo-2-((1-trityl-1H-imidazol-4-yl)methyl)quinoxaline-6-carboxamide
4h	(S)-2-(4-tert-butoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
4i	(S)-2-Benzyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
4k	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isobutyl-3-oxoquinoxaline-6-carboxamide
4l	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-((1-methyl-1-H-indol-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide
5c	(S)-2-((1H-indol-3-yl)methyl)-N-(2-aminophenyl)-1,2,3,4-tetrahydro-3-oxoquinoxaline-6-carboxamide

Cpd No.	Compound
6l	(S)-2-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide
8	(S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3 oxoquinoxaline-6-carboxamide
11	(S)-N-(5-(Hydroxycarbamoyl)pentyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxamide
16a	(S)-1-(4-fluorobenzyl)-N-hydroxy-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
16b	(S)-1-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide
16c	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-(3-phenylpropyl)quinoxaline-6-carboxamide
16d	4-(((S)-7-(hydroxycarbamoyl)-2,3-dihydro-3-isopropyl-2-oxoquinoxalin-4(1H)-yl)methyl)benzoic acid
16e	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-((thiophen-2-yl)methyl)quinoxaline-6-carboxamide
16f	(S)-N-hydroxy-1-(4-(N-hydroxycarbamimidoyl)benzyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
16g	(S)-1-benzyl-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide
16h	(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-1-((naphthalen-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide
18a	(S)-N-hydroxy-2-isopropyl-3-oxo-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
18b	(S)-N-hydroxy-1-(biphenyl-4-sulfonyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
18c	(S)-N-hydroxy-2-isopropyl-3-oxo-1-(2,4,6-trimethybenzenesulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
18e	(S)-N-hydroxy-1-(4-methoxybenzenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
18f	(S)-N-hydroxy-1-(1-naphthalenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
23a	N1-(2-Aminophenyl)-N8-((S)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)octanediamide
24a	N1-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide
24e	N1-((R)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide
24f	N1-((R)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide
26e	N1-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide
29a	N-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-8-(oxazol-2-yl)-8-oxooctanamide
43	6-((R)-1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxy-4-oxy-hexanamide
47a	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxyhexanamide
47b	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-aminophenyl)hexanamide
49	6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)hexanamide

Cpd No.	Compound
$54a_1$	4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide
$54a_2$	4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide
$54b_1$	N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-benzamide
$54b_2$	(R)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_3$	(S)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_4$	(S)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_5$	(R)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_6$	N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
$54b_7$	(R)-N-hydroxy-4-((3-oxo-2-phenethyl-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
$54b_8$	(R)-4-((2-(cyclohexylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_9$	(R)-tert-butyl 4-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)butylcarbamate
$54b_{10}$	(R)-N-hydroxy-4-((2-(naphthalen-2-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
$54b_{11}$	(R)-4-((2-(4-tert-butoxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{12}$	(R)-tert-butyl 3-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)propanoate
$54b_{13}$	(R)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{14}$	(S)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{15}$	(R)-4-((2-(4-fluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{16}$	(R)-4-((2-(3,4-difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{17}$	(R)-4-((2-(4-trifluoromethylbenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{18}$	(R)-N-hydroxy-4-((2-(4-hydroxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
$54b_{19}$	(R)-N-hydroxy-4-((2-(3-(trifluoromethyl)benzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
$54b_{20}$	(R)-4-((2-(furan-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide
$54b_{21}$	(R)-N-hydroxy-4-((3-oxo-2-(pyridin-3-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
54c	(S)-N-(2-aminophenyl)-4-((3-oxo-2-(thiophen-2-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide
56a	4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide
62	4-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)benzamide
66c	(E)-3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide
66f	(E)-3-((R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide

Cpd No.	Compound
$68b_1$	6-((S)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_3$	6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_4$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_6$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_7$	6-((S)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_8$	6-((R)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_9$	6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{11}$	6-((S)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{12}$	6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{16}$	6-(3,3-spirocyclopentyl-2,5-dioxo-2,3,4,5,tetrahydrobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{17}$	6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{18}$	6-((R)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{19}$	6-((S)-3-cyclohexyl-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{20}$	6-((S)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{21}$	6-((R)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{22}$	6-((S)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
$68b_{23}$	6-((R)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide
69	3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxypropanamide
71	N-(2-aminophenyl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide
72	N-(4-aminothiophen-3-yl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide
74	6-(2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
79	6-(1-(2-(1H-indol-3-yl)ethyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
80	6-(1-benzyl-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
81	6-(1-(3,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
82	6-(1-(4-methoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
83	6-(2,3,4,5-tetrahydro-2,5-dioxo-1-phenethyl-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
88a	6-(2,3,4,5-tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide

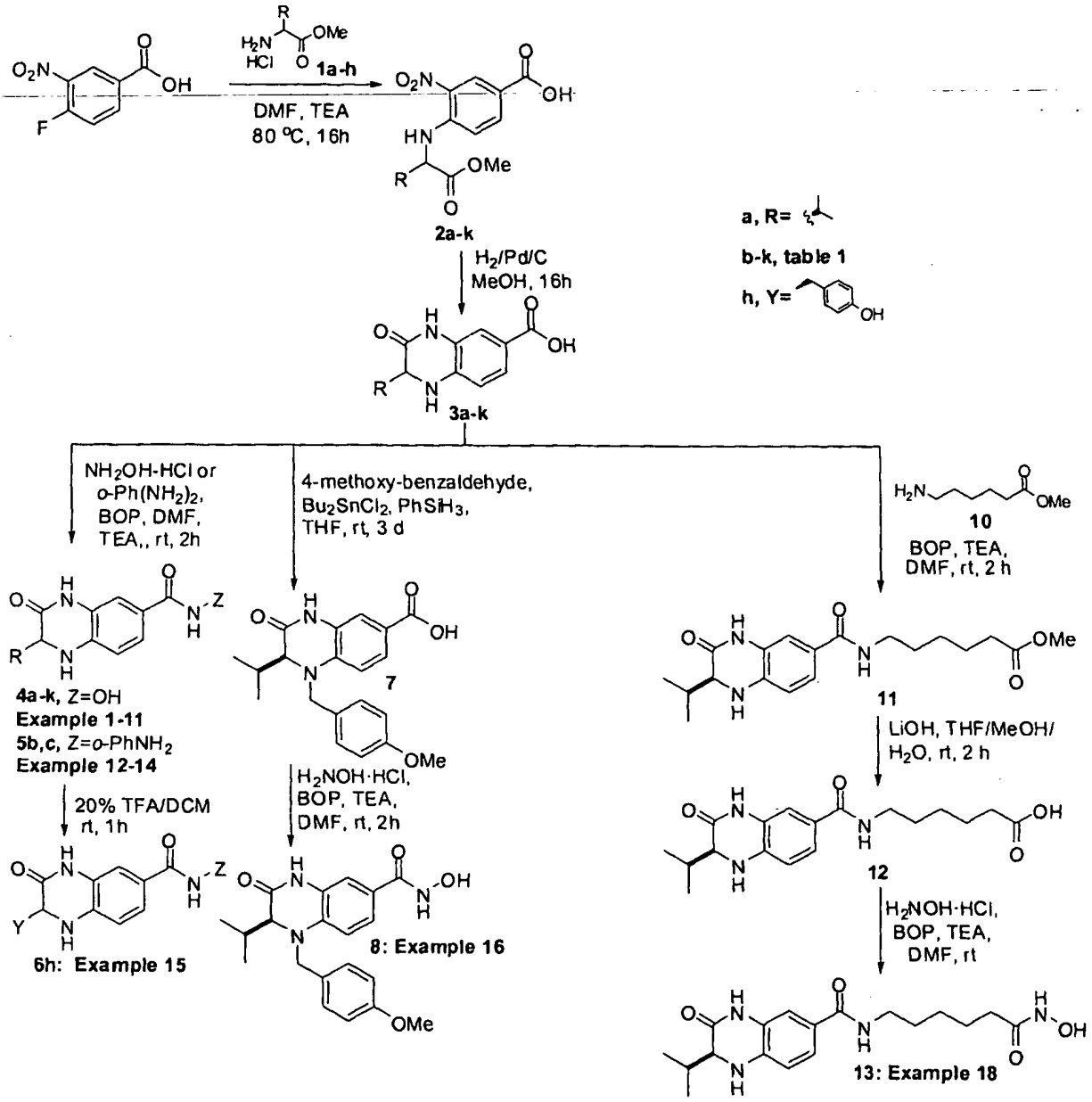
Cpd No.	Compound
92a	6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide
92b	(S)-benzyl 3-(6-(hydroxyamino)-6-oxohexyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-7-ylcarbamate
97a	(R)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97b	(S)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97c	(S)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97d	(R)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97f	(R)-N-hydroxy-3-isobutyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97g	(R)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97h	(S)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97i	(S)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97j	(R)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
97k	N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide
109a	(2S,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate
109b	(2S,4R)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate
109c	(2R,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate
112a	(2S,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate
112b	(2S,4R)-benzyl 4-(2-(hydroxyamino)-2-oxoethoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate
112c	(2R,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate

Synthetic Schemes and Experimental Procedures

[0110] The compounds of the invention can be prepared according to the reaction schemes for the examples illustrated below utilizing methods known to one of ordinary skill in the art. These Schemes serve to exemplify some procedures that can be used to make the compounds of the invention. One skilled in the art will recognize that other general synthetic procedures may be used. The compounds of the invention can be prepared from starting components that are commercially available. Any kind of substitutions can be made to the starting components to obtain the compounds of the invention according to procedures that are well known to those skilled in the art.

[0111] The present invention will be more readily understood by referring to the following examples, which are given to illustrate the invention rather than to limit its scope.

Scheme 1



Example 1

(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide (Compound 4a)

Step 1: 4-((S)-1-(Methoxycarbonyl)-2-methylpropylamino)-3-nitrobenzoic acid (Compound 2a)

[0112] Both (L)-valine methyl ester hydrochloride (1.54 g, 9.19 mmol) (**1a**) and 4-fluoro-3-nitrobenzoic acid (1.70 g, 9.19 mmol) were dissolved in DMF (10 mL) at room temperature. Triethylamine (3.84 mL, 27.6 mmol) was then added, and the resulting solution heated to 80°C for 16 h. After cooling, the solution was filtered, and the solvent removed. The residue, acid **2a**, was obtained in near quantitative yield, and used in the subsequent reaction without further purification. LRMS (ESI): (calc.) 296.3; (found) 297.1 $(MH)^+$.

Step 2: (S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxylic acid (Compound **3a**)

[0113] Acid **2a** (2.72 g, 9.19 mmol) was dissolved in MeOH (50 mL), and 10% Pd/C (982 mg, 0.919 mmol) was added to the resulting solution. After stirring for 16 h under a hydrogen atmosphere, the solution was filtered through a pad of celite, and the filtrate concentrated. After purification of the residue by flash chromatography (eluent 0-80% EtOAc in hexanes), 1.83 g (85%) of Compound **3a** was obtained as a light yellow crystalline solid. LRMS (ESI): (calc.) 234.3; (found) 235.4 $(MH)^+$.

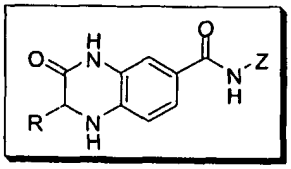
Step 3: (S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide (Compound **4a**)

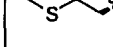
[0114] Acid **3a** (237 mg, 1.01 mmol) was dissolved in DMF (4 mL), and BOP (535 mg, 1.21 mmol) was added in one portion. After stirring for 5 min, hydroxylamine hydrochloride (84 mg, 1.21 mmol) was added, followed by the addition of triethylamine (0.56 mL, 4.04 mmol). The resulting solution was stirred for 2 h prior to the removal of all solvents. After purification of the residue by flash chromatography (eluent 0-20% MeOH in EtOAc), 86 mg (34%) of Compound **4a** was obtained as a light pink crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.37 (s, 1H), 8.79 (br s, 1H), 7.18 (s,1H), 7.15 (s, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.51 (br s,1H), 3.68 (d, J = 3.1 Hz, 1H), 3.38 (br s, 1H), 2.00-2.10 (m, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.7 Hz, 3H). LRMS (ESI): (calc.) 249.3; (found) 250.1 $(MH)^+$.

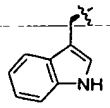
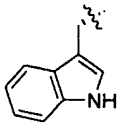
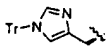
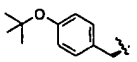
Examples 2-14

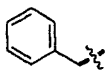
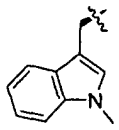
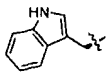
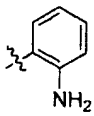
[0115] Examples 2-13 describe the preparation of Compounds **4b-k** and **5b-c** using the same procedures as described for Compound **4a** in Example 1. Characterization data are presented in Table 2.

Table 2



Ex.	Cpd.	R	Z	Name	Characterization	Scheme
2	4b		-OH	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-(2-(methylthio)ethyl)-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.97 (s, 1H), 7.27 (dd, J = 8.2, 2.0 Hz, 1H), 7.19 (d, J = 1.7 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 4.12-4.09 (m, 1H), 3.33 (t, J = 1.6 Hz, 2H), 2.88 (s, 2H), 2.09 (s, 3H). **LRMS** (ESI): (calc.) 281.1; (found) 282.1 $(MH)^+$.	1

Ex.	Cpd.	R	Z	Name	Characterization	Scheme
3	4c		-OH	(S)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.52 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.18 (dd, J = 8.2, 2.0 Hz, 1H), 7.09 - 6.96 (m, 4H), 6.57 (d, J = 8.2 Hz, 1H), 4.22 (dd, J = 8.2, 3.9 Hz, 1H), 3.31 - 3.17 (m, 2H). **LRMS** (ESI): (calc.) 336.2; (found) 337.2 $(MH)^+$.	1
4	4d		-OH	(S)-2-sec-Butyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.75 (br s, 1H), 10.32 (s, 1H), 8.93 (br s, 1H), 7.12-7.11 (m, 2H), 6.62 (d, J = 8.0 Hz, 1H), 6.50 (d, J = 1.6 Hz, 1H), 3.73-3.72 (m, 1H), 1.78-1.74 (m, 1H), 1.46 - 1.40 (m, 1H), 1.15-1.08 (m, 1H), 0.90 (d, J = 7.0 Hz, 3H), 0.81 (t, J = 7.4 Hz, 3H). **LRMS** (ESI): (calc.) 358.2; (found) 359.2 $(MH)^+$.	1
5	4e		-OH	(R)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.23 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 7.14 (d, J = 2.0 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 3.77 (d, J = 4.8 Hz, 1H), 2.16-2.06 (m, 1H), 1.02 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H). **LRMS** (ESI): (calc.) 249.1; (found) 250.1 $(MH)^+$.	1
6	4f		-OH	(R)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.82 (br s, 1H), 10.77 (br s, 1H), 10.39 (br s, 1H), 8.70 (br s, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.13 - 7.11 (m, 2H), 7.07 (d, J = 2.4 Hz, 1H), 7.02 (t, J = 7.9 Hz, 1H), 6.58 (d, J = 8.8 Hz, 1H), 6.33 (s, 1H), 4.14-4.11 (m, 1H), 3.09 - 2.95 (m, 2H). **LRMS** (ESI): (calc.) 336.1; (found) 337.1 $(MH)^+$.	1
7	4g		-OH	(S)-1,2,3,4-Tetrahydro-N-hydroxy-3-oxo-2-((1-trityl-1H-imidazol-4-yl)methyl)quinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.78 (br s, 1H), 10.31 (s, 1H), 8.71 (br s, 1H), 7.37-7.30 (m, 9H), 7.18 (d, J = 1.4 Hz, 1H), 7.13-7.10 (m, 2H), 7.03-7.00 (m, 6H), 6.56 (d, J = 1.4 Hz, 1H), 6.48 (d, J = 8.4 Hz, 1H), 6.34 (s, 1H), 4.08-4.07 (m, 1H), 2.78-2.72 (m, 2H). **LRMS** (ESI): (calc.) 529.1; (found) 530.1 $(MH)^+$.	1
8	4h		-OH	(S)-2-(4-tert-Butoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.77 (s, 1H), 10.32 (s, 1H), 8.68 (br s, 1H), 7.14-7.04 (m, 4H), 6.78 (d, J = 7.5 Hz, 2H), 6.58 (d, J = 8.5 Hz, 1H), 6.43 (s, 1H), 4.11-4.13 (m, 1H), 2.88-2.85 (m, 2H), 1.20 (s, 9H).	1

Ex.	Cpd.	R	Z	Name	Characterization	Scheme
9	4i		-OH	(S)-2-Benzyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.83 (br s, 1H), 10.38 (s, 1H), 8.76 (br s, 1H), 7.27 (d, *J* = 6.3 Hz, 2H), 7.15-7.24 (m, 4H), 7.14 (d, *J* = 1.8 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.46 (br s, 1H), 4.18 (t, *J* = 4.5 Hz, 1H), 2.90-3.00 (m, 2H). **LRMS** (ESI): (calc.) 297.3; (found) 298.1 $(MH)^+$.	1
11	4k		-OH	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isobutyl-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.84 (s, 1H), 10.34 (s, 1H), 7.19 (d, *J* = 1.8 Hz, 2H), 6.70 (d, *J* = 8.6 Hz, 1H), 6.50 (br s, 1H), 3.83 (t, *J* = 5.7 Hz, 1H), 1.80-1.90 (m, 1H), 1.42-1.52 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 6H) **LRMS** (ESI): (calc.) 263.3; (found) 264.1 $(MH)^+$.	1
12	4l		-OH	(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-((1-methyl-1-H-indol-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR (DMSO-d_6)□ δ ppm:** 10.88 (bs, 1H), 10.42 (s, 1H), 8.81 (s, 1H), 7.61 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.24-7.16 (m, 4H), 7.08 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.46 (s, 1H), 4.21 (s, 1H), 3.81 (s, 3H), 3.17 (dd, J = 4.1, 10.4Hz, 1H), 3.07 (dd, J = 7.4, 7.0 Hz, 1H). **LRMS** (ESI): (calc.) 350.37; (found) 351 $(MH)^+$.	Steps 1-2 (ex.1), steps 1 and 3 (Ex.19)
14	5c			(S)-2-((1H-Indol-3-yl)methyl)-N-(2-aminophenyl)-1,2,3,4-tetrahydro-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.84 (s, 1H), 10.35 (s, 1H), 9.30 (s, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.43 (d, J = 10.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.27 (s, 1H), 7.11-7.09 (m, 2H), 7.04 (t, J = 6.9 Hz, 1H), 6.97 - 6.89 (m, 2H), 6.73 (d, J = 8.2 Hz, 1H), 6.65 (d, J = 8.2 Hz, 1H), 6.56 (t, J = 7.2 Hz, 1H), 6.44 (s, 1H), 4.80 (br s, 2H), 4.17-4.15 (m, 1H), 3.07-2.98 (m, 2H). **LRMS** (ESI): (calc.) 411.2; (found) 412.4 $(MH)^+$.	1

Example 15

(S)-2-(4-Hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide (Compound 6h)

Step1-3: (S)-2-(4-tert-Butoxybenzyl)-N-hydroxy-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide (Compound **4h**)

[0116] Following the same procedure Example 1, step 1-3, Compound **4a**, but substituting **3h** for **3a**, the title Compound **4h** was obtained in 36% yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.77 (s, 1H), 10.32 (s, 1H), 8.68 (br s, 1H), 7.14-7.04 (m, 4H), 6.78 (d, J = 7.5 Hz, 2H), 6.58 (d, J = 8.5 Hz, 1H), 6.43 (s, 1H), 4.11-4.13 (m, 1H), 2.88-2.85 (m, 2H), 1.20 (s, 9H). LRMS (ESI): (calc.) 369.1; (found) 314.0 $(M\text{-}tBu)^+$.

Step 4: (S)-2-(4-Hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide (Compound **6h**)

[0117] To a stirred solution of **4h** (75 mg, 0.2 mmol) in DCM (15 mL) was added concentrated trifluroacetic acid (3 mL). The solution was stirred for 1 h and then diluted with water (10 mL). Aqueous extraction was performed with DCM (2 x 10 mL) and EtOAc (10 mL). The organic layers were concentrated and the residue was purified by preparative reverse phase HPLC (aquasil C-18, 100X4.6, 5uM) with MeOH (15-95 %) in H_2O to afford the title Compound **6h** as a yellow solid (15 mg, 24%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.80 (s, 1H), 10.31 (s, 1H), 9.18 (s, 1H), 8.71 (s, 1H), 7.13-7.11 (m, 2H), 6.94 (d, J = 7.5 Hz, 2H), 6.61-6.60 (m, 3H), 6.31 (s, 1H), 4.02-3.99 (m, 1H), 2.81-2.71 (m, 2H). LRMS (ESI): (calc.) 313.0; (found) 314.0 $(MH)^+$.

Example 16

(S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3 oxoquinoxaline-6-carboxamide (Compound 8)

Step 3: (S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxylic acid (Compound **7**)

[0118] Acid **3a** (see Example 1, Compound **4a**, steps 1-2, Scheme 1 for preparation) (130 mg, 0.555 mmol), 4-methoxy-benzaldehyde (0.070 mL, 0.555 mmol), dibutyltin dichloride (17 mg, 0.056 mmol) and phenyl silane (0.08 mL, 0.610 mmol) were all dissolved in THF/DMF (2:1, 3 mL), and the resulting solution stirred for 3 days. Following removal of the solvent and purification of the residue by flash chromatography (eluent 0-100% EtOAc in hexanes), 114 mg (58%) of Compound **7** was obtained as a white crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 12.28 (br s,1H), 10.62 (br s,1H), 7.40 (d, J = 8.6 Hz, 1H), 7.36 (s,1H), 7.19 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.3 Hz, 2H), 6.77 (d, J = 8.6 Hz, 1H), 4.83 (d, J = 15.5 Hz, 1H), 4.44 (d, J = 15.3 Hz, 1H), 3.82 (d, J = 5.9 Hz, 1H), 3.74 (s,3H), 1.92-2.02 (m,1H), 0.94 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H). LRMS (ESI): (calc.) 354.4; (found) 355.1 $(MH)^+$.

Step 4: (S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide (Compound **8**)

[0119] Following the procedure described in Example **4a**, step 3 (Scheme 1) but substituting acid **7** for acid **3a**, the title Compound **8** was obtained in 39% yield as a white crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.85 (br s,1H), 10.57 (br s,1H), 8.79 (br s,1H), 7.18 (m, 4H), 6.88 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 4.82 (d, J = 15.7 Hz, 1H), 4.42 (d, J = 15.7 Hz, 1H), 3.78 (d, J = 6.1 Hz, 1H), 3.73 (s, 3H), 1.90-2.00 (m, 1H), 0.93 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.3 Hz, 3H). LRMS (ESI): (calc.) 369.4; (found) 370.2 $(MH)^+$.

Example 18

(S)-N-(5-(Hydroxycarbamoyl)pentyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxamide (Compound 13)

Step 3: (S)-Methyl 6-(2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamido)hexanoate (Compound **11**)

[0120] Acid **3a** (see Example **1** (Compound **4a**), steps 1-2, Scheme 1 for preparation) (356 mg, 1.52 mmol) was dissolved in DMF (5 mL), and BOP (805 mg, 1.82 mmol) was subsequently added in one portion. After stirring at room temperature for 5 min, 6-amino-hexanoic acid methyl ester **10** (331 mg, 1.82 mmol) was added, followed by the addition of triethylamine (1.06 mL, 7.60 mmol). The resulting solution was stirred for 2 h prior to the removal of the solvent. After purification of the residue by flash chromatography (eluent 0-100% EtOAc in hexanes), Compound **11** was obtained as a light yellow crystalline solid (547 mg, 99%). LRMS (ESI): (calc.) 361.4; (found) 362.1 $(MH)^+$.

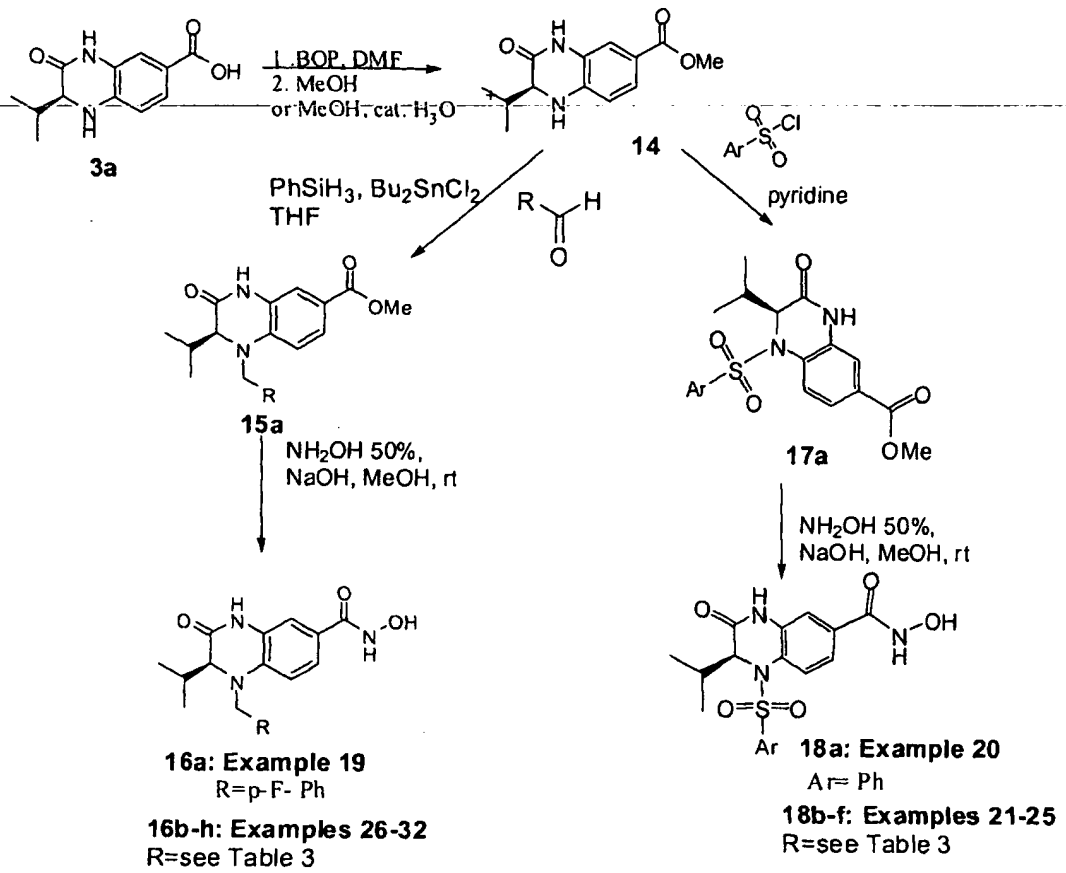
Step 4 :(S)-6-(2-Isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamido)-hexanoic acid (Compound **12**)

[0121] Methyl ester **11** (547 mg, 1.50 mmol) was dissolved in THF/MeOH/H_2O (1:2:1, 4 mL), and lithium hydroxide monohydrate (319 mg, 7.20 mmol) was added to the resulting solution. After stirring at room temperature for 2 h, the solution was acidified to pH = 6 with HCl, and extracted from brine with EtOAc. Following purification of the residue by flash chromatography (eluent 0-100% EtOAc in hexanes), 428 mg (81%) of Compound **12** was obtained as a light yellow crystalline solid. LRMS (ESI): (calc.) 347.4; (found) 348.6 $(MH)^+$.

Step 5: (S)-N-(5-(Hydroxycarbamoyl)pentyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxamide (Compound **13**)

[0122] Following the procedure described in Example 1, Compound **4a**, step 3 (Scheme 1) but substituting acid **12** for acid **3a**, the title Compound was obtained in 44% yield as a light yellow crystalline solid. ^1H NMR: (DMSO-d_6) δ (ppm): 10.34 (br s, 1H), 8.67 (br s, 1H), 8.03 (br s, 1H), 7.27 (d, J = 8.2 Hz, 1H), 7.21 (s, 1H), 6.69 (d, J = 8.2 Hz, 1H), 6.52 (s, 1H), 3.69 (d, J = 2.7 Hz, 1H), 3.35 (s, 1H), 3.14-3.24 (m, 2H), 2.00-2.10 (m, 1H), 1.97 (t, J = 7.3 Hz, 2H), 1.42-1.60 (m, 4H), 1.24-1.34 (m, 2H), 0.97 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H). LRMS (ESI): (calc.) 362.4; (found) 363.1 $(MH)^+$.

Scheme 2



Example 19

(S)-1-(4-Fluorobenzyl)-N-hydroxy-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide (Compound 16a)

Step 1: (S)-Methyl-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxylate (Compound **14**)

[0123] Acid **3a** (see Example 1 (Compound **4a**), steps 1-2, Scheme 1 for preparation) (1.5 g, 6.40 mmol) and BOP (1.813 g, 4.098 mmol) were dissolved in DMF (4 mL). Reaction was stirred for 3 h. The reaction was quenched with MeOH (4mL) and stirred for 16 h. EtOAc (10 mL) was added, and the organic phase was washed twice with $NaHCO_3$, and once with brine. The organic layer was dried over $MgSO_4$, filtered and concentrated. The title Compound **14** was obtained as white solid by crystallization from MeOH (1.34 g, 84%). ^1H NMR: (DMSO-d_6) δ (ppm): 10.46 (s, 1H), 7.43 (dd, J = 2, 6.5 Hz, 1H), 7.33 (d, J = 2 Hz, 1H), 6.91 (s, 1H), 6.78 (d, J = 8.4 Hz, 1H), 3.83 (dd, J = 2.2, 1 Hz), 3.79 (s, 3H), 2.15-2.09 (m, 1H), 1.01 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H).

Step 2: (S)-Methyl 1-(4-fluorobenzyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydro-quinoxaline-6-carboxylate (Compound **15a**)

[0124] Following the procedure described in Example 16, step 3 (Scheme 1) but substituting **14** for acid **3a**, the title Compound **15** was obtained and used in the following step without further purification.

Step 3: (S)-1-(4-Fluorobenzyl)-N-hydroxy-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide (Compound **16a**)

[0125] To the reaction mixture of **15a**, NH_2OH 50% wt solution (1 mL) and 1N NaOH (5 eq.) was added and stirred for 2 h. The reaction mixture was concentrated and the residue was purified by preparative reverse phase HPLC (aquasil C-18, 100X4.6, 5uM) with MeOH (10-95%) in H_2O to afford the title Compound **16a**.

[0126] The title Compound **16a** was obtained as white solid (7 mg, 10%). ^1H NMR (CD_3OD) δ ppm: 7.28-7.25 (m, 2H), 7.22 (bs, 1H), 7.02 (t, J = 8.8 Hz, 2H), 6.75 (d, J = 7.8 Hz, 1H), 4.47 (d, J = 15.7 Hz, 1H), 3.75 (d, 6.5 Hz, 1H), 2.05-2.0 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). LRMS (ESI): (calc.) 357.38; (found) 358 $(MH)^+$.

Example 20

(S)-N-Hydroxy-2-isopropyl-3-oxo-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide (Compound 18a)

Step 2: (S)-Methyl 2-isopropyl-3-oxo-1-(phenylsulfonyl)-1,2,3,4-tetrahydro-quinoxaline-6-carboxylate (Compound **17a**)

[0127] General Procedure for the Preparation of sulfonamides: Methyl ester **14** (500 mg, 2.0 mmol) and benzenesulfonyl chloride (1.13 g, 6.4 mmol) were stirred in pyridine (2 mL) at room temperature and the progress of the reaction is followed by MS and TLC. After 16 h, pyridine was removed under reduced pressure and the crude product was purified by column chromatography eluting with 40% EtOAc in hexanes to give **17a** in 81% yield. LRMS (ESI): (calc.) 388.4; (found) 389.1 $(MH)^+$.

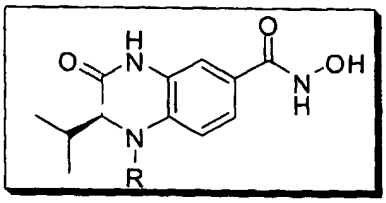
Step 3: (S)-N-Hydroxy-1-benzenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide (Compound **18a**)

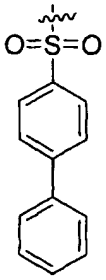
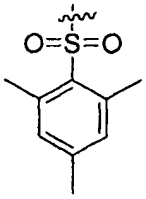
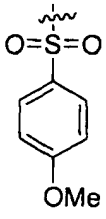
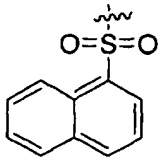
[0128] Following the procedure described in Example 19, step 3 (Scheme 2) but substituting methyl ester **17a** for **15a**, the title Compound **18a** was obtained as a pink solid (20 mg, 30%). ^1H NMR: (DMSO-d_6) δ (ppm): 10.39 (s, 1H), 7.59 (m, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.35 (d, J = 8.2 Hz, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.1 (s, 1H), 3.98 (d, J = 9.6 Hz, 1H), 1.45-1.38 (m, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H).

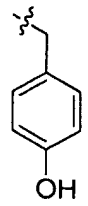
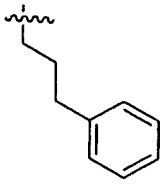
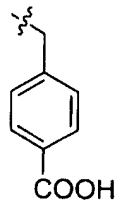
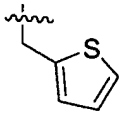
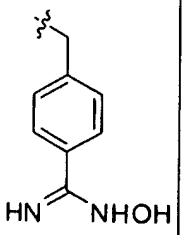
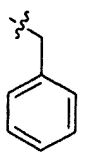
Examples 21-32

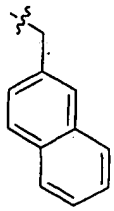
[0129] Examples 21-32 describe the preparation of Compound **16** (b-h) and **18** (b-f), using the same procedures as described for Compound **16a** in Example 19 or Compound **18a** in Example 20. Characterization data are presented in Table 3.

Table 3

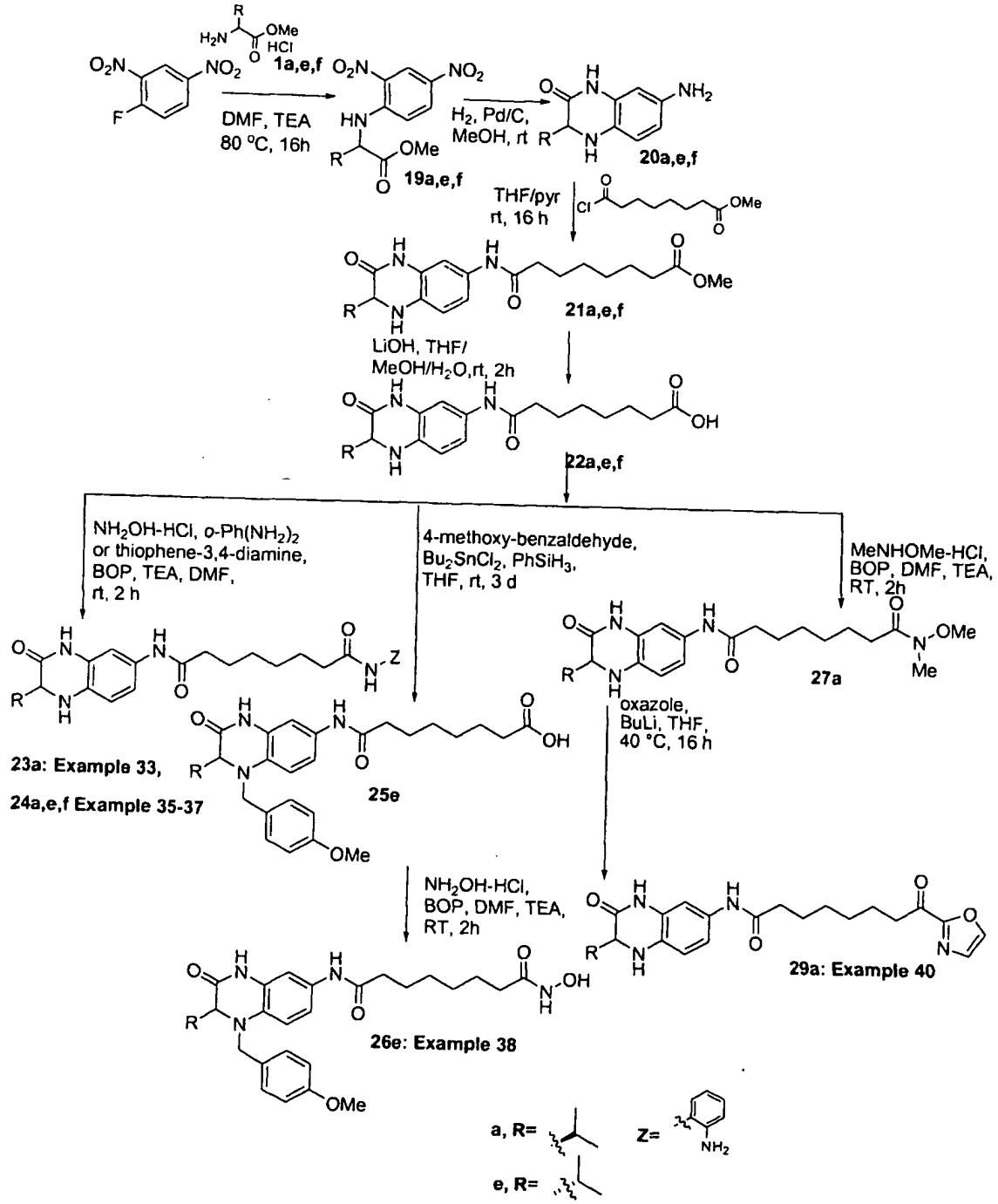


Ex	Cpd	R	Name	Characterization	Scheme
21	18b		(S)-N-Hydroxy-1-(biphenyl-4-sulfonyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 10.53 (b, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.7 (d, J = 7.0Hz, 2H), 7.65 (d, J = 8.2 Hz, 1H), 7.48-7.41 (m, 6H), 7.19 (d, J = 2Hz, 1H), 4.09 (d, J = 9.6 Hz, 1H), 1.54-1.47 (m, 1H), 0.93 (d, J = 6.7, Hz, 3H), 0.91 (d, J = 6.7, Hz, 3H). **LRMS** (ESI): (calc.) 465.5; (found) 466 $(MH)^+$.	2
22	18c		(S)-N-Hydroxy-2-isopropyl-3-oxo-1-(2,4,6-trimethybenzenesulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 10.67 (b, 1H), 7.29 (dd, J = 8.4, 15.0 Hz, 2H), 7.21 (s, 1H), 6.97 (s, 2H), 3.75 (d, J = 9.6 Hz, 1H), 2.30 (s, 6H), 2.18 (s, 3H), 1.46-1.41 (m, 1H), 0.81 (d, J = 6.7 Hz, 3H), 0.75 (d, J = 6.5 Hz, 3H). LRMS (ESI): (calc.) 431.5; (found) 432 $(MH)^+$.	2
24	18e		(S)-N-Hydroxy-1-(4-methoxybenzenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 10.50 (b, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.4 (dd, J = 1.8, 6.5 Hz, 1H), 7.28 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 1.8 Hz, 1H), 6.99 (d, J = 8.8 Hz, 2H), 4.03 (d, J = 9.6 Hz, 1H), 3.78 (s, 3H), 1.51-1.44 (m, 1H), 0.92 (d, J = 6.7, Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H). LRMS (ESI): (calc.) 407.42; (found) 408 $(MH)^+$.	2
25	18f		(S)-N-Hydroxy-1-(1-naphthalenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 10.21 (s, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.14 (dd, J = 1, 6.5 Hz, 1H), 8.0 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.52 (t, J = 6.8 Hz, 1H), 7.44 (dd, J = 2, 6.5 Hz, 1H), 7.26-7.21 (m, 1H), 6.95 (d, J = 2 Hz, 1H), 4.06 (d, J = 9.6 Hz, 1H), 1.53-1.47 (m, 1H), 0.91 (d, J = 6.5, Hz, 3H), 0.90 (d, J = 6.7, Hz, 3H). **LRMS** (ESI): (calc.) 439.5; (found) 440 $(MH)^+$.	2

Ex	Cpd	R	Name	Characterization	Scheme
26	16b		(S)-1-(4-Hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.17 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 1.6 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 8.6 Hz, 1H), 6.59 (d, J = 8.6 Hz, 2H), 4.68 (d, J = 14.9 Hz, 1H), 4.24 (d, J = 15 Hz, 1H), 3.59 (d, J = 6.5 Hz, 1H), 1.85-1.93 (m, 1H), 0.92 (d, J = 6.8, Hz, 3H), 0.88 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc.) 355.4; (found) 356 $(MH)^+$.	2
27	16c		(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-(3-phenylpropyl)quinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.33 (dd, J = 8.4,1.4 Hz, 1H), 7.25-7.12 (m, 8H), 6.71 (d, J = 8.6 Hz, 1H), 3.83-3.77 (m, 1H), 3.63 (d, J = 6.7 Hz, 2H), 3.20-3.14 (m, 1H), 2.64-2.6 (m, 1H), 2.0-1.88 (m, 1H), 0.85 (d, J = 6.8, Hz, 3H), 0.78 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc.) 367.4; (found) 368 $(MH)^+$.	2
28	16d		4-(((S)-7-(Hydroxycarbamoyl)-2,3-dihydro-3-isopropyl-2-oxoquinoxalin-4(1H)-yl)methyl)benzoic acid	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.91 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H), 6.72 (d, J = 8.6 Hz, 2H), 4.95 (d, J = 9 Hz, 1H), 4.57 (d, J = 0.2 Hz, 1H), 3.81 (d, J = 6.3 Hz, 1H), 2.08- 2.03 (m, 1H), 1.01 (d, J = 6.8, Hz, 3H), 0.94 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc.) 383.3; (found) 384 $(MH)^+$.	2
29	16e		(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-((thiophen-2-yl)methyl)quinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.32 (d, J = 9 Hz, 1H), 7.26 (d, J = 4.1 Hz, 1H), 7.22 (s, 1H), 7.02 (d, J = 3.5 Hz, 1H), 6.94-6.91 (m, 2H), 5.11 (d, J = 16.0 Hz, 1H), 4.63 (d, J = 15.7 Hz, 1H), 3.77 (d, J = 6.5 Hz, 1H), 1.99-1.98 (m, 1H), 0.98 (d, J = 6.8, Hz, 3H), 0.91 (d, J = 6.7, Hz, 3H). **LRMS** (ESI): (calc.) 345.4; (found) 346 $(MH)^+$.	2
30	16f		(S)-N-hydroxy-1-(4-(N-hydroxycarbamimidoyl)benzyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.56 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.24-7.22 (m, 2H), 6.73 (d, J = 8.2 Hz, 1H), 5.0 (d, J= 16.4 Hz, 1H, overlapped with water signal), 4.54 (d, J = 16.2 Hz, 1H), 3.8 (d, J = 6.3 Hz, 1H), 2.07-2.0 (m, 1H), 1.00 (d, J = 6.8, Hz, 3H), 0.94 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc.) 397.4; (found) 398 $(MH)^+$.	2
31	16g		(S)-1-Benzyl-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.19-7.08 (m, 7H), 6.65 (d, J = 8.4 Hz, 1H), 4.37 (d, J = 15.8 Hz, 1H), 3.64 (d, J = 6.3 Hz, 1H), 1.96-1.88 (m, 1H), 0.90 (d, J = 6.7, Hz, 3H), 0.83 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc.) 339.4; (found) 340 $(MH)^+$.	2

Ex	Cpd	R	Name	Characterization	Scheme
32	16h		(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-1-((naphthalen-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide	^{1}H NMR: (MeOD-d_4) δ (ppm): 10.78 (bs, 1H), 10.58 (s, 1H), 8.76 (bs, 1H), 7.84-7.77 (m, 4H), 7.48-7.43 (m, 2H), 7.36 (d, J = 8.4 Hz, 1H), 7.20 (s, 1H), 7.12 (d, J = 6.7 Hz, 1H), 5.01 (d, J = 15.8 Hz, 1H), 4.65 (d, 16.2 Hz, 1H), 3.84 (d, 6.5 Hz, 1H), 1.99-1.93 (m, 1H), 0.94 (d, J = 7.0, Hz, 3H), 0.86 (d, J = 6.8, Hz, 3H). **LRMS** (ESI): (calc) 389.5; (found) 390 $(MH)^+$.	2

Scheme 3



Example 33

N1-(2-Aminophenyl)-N8-((S)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)octanediamide (Compound 23a)

Step 1: (S)-Methyl 2-(2,4-dinitrophenylamino)-3-methylbutanoate (Compound **19a**)

[0130] Following the procedure described in Example 1, Compound **4a**, step 1 (Scheme 1) but substituting 1-fluoro-2,4-dinitrobenzene for 4-fluoro-3-nitrobenzoic acid, the title Compound **19a** was obtained in near quantitative yield, and used in the subsequent reaction without further purification. LRMS (ESI): (calc.) 297.3; (found) 298.1 $(MH)^+$.

Step 2: (S)-7-Amino-3,4-dihydro-3-isopropylquinoxalin-2(1*H*)-one (Compound **20a**):

[0131] Following the procedure described in Example 1, **4a**, step 2 (Scheme 1) but substituting Compound **19a** for **2a**, the title Compound **20a** was obtained in 88% yield as a light brown crystalline solid. LRMS (ESI): (calc.) 205.3; (found) 206.2 $(MH)^+$.

Step 3: Methyl 7-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-ylcarbamoyl)-heptanoate (Compound **21a**)

[0132] Aniline **20a** (508 mg, 2.48 mmol) was dissolved in THF/pyridine (2:1, 6 mL), followed by the addition of methyl 7-chlorocarbonyl-heptanate (0.387 mL, 2.72 mmol). After stirring for 16 h at room temperature, the solvent was removed. The residue was purified by flash chromatography (eluent 0-80% EtOAc in hexanes) to afford Compound **21a** as a light pink crystalline solid (247 mg, 27%). LRMS (ESI): (calc.) 375.5; (found) 376.1 $(MH)^+$.

Step 4: 7-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-ylcarbamoyl)-heptanoic acid (Compound **22a**)

[0133] Following the procedure described in Example **18**, step 4 (Scheme 1) but substituting methyl ester **21a** for **11**, the title Compound **22a** was obtained in 76% yield as a light yellow crystalline solid. LRMS (ESI): (calc.) 361.4; (found) 362.3 $(MH)^+$.

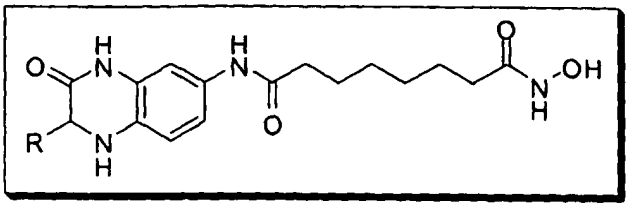
Step 5: N1-(2-Aminophenyl)-N8-((S)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)octanediamide (Compound 23a)

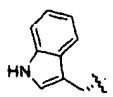
[0134] Following the procedure described in Example 1, Compound **4a**, step 3 (Scheme 1) but substituting acid **22a** for acid **3a**, and benzene-1,2-diamine for hydroxylamine hydrochloride, the title Compound **23a** was isolated in 71% yield as a light yellow crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 12.25 (br s,1H), 10.21 (br s, 1H), 9.11 (br s, 1H), 7.96 (br s,2H), 7.86 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 6.88 (t, J = 7.6 Hz, 1H), 6.72 (d, J = 7.6 Hz, 1H), 6.54 (t, J = 7.2 Hz, 1H), 4.84 (s, 1H), 2.55 (d, J = 9.4 Hz, 1H), 3.44 (m, 1H), 2.34 (m, 4H), 1.64 (m, 4H), 1.38 (m, 4H), 1.23 (d, J = 6.7 Hz, 6H). LRMS (ESI): (calc.) 451.6; (found) 450.5 $(MH)^+$.

Examples 34-37

[0135] Examples 34-37 describe the preparation of Compound **23a2**, **24a**, **24e** and **24f** using the same procedures as described for Compound **23a1** in Example 33. Characterization data are presented in Table 4.

Table 4



Ex.	Cpd.	R	Name	Characterization	Scheme
35	24a		N1-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm)**:10.43 (br s,1H), 8.73 (br s,1H), 7.89 (s,1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 2.39 (t, *J* = 7.4 Hz, 2H), 3.44 (m, 1H), 1.94-2.01 (m, 2H), 1.58-1.66 (m, 2H), 1.45-1.56 (m, 2H), 1.28-1.36 (m, 4H), 1.23 (d, *J* = 6.8 Hz, 6H). **LRMS** (ESI): (calc.) 376.5; (found) 375.4 $(MH)^+$.	3
36	24e		N1-((R)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm)**: 12.25 (br s,1H), 10.35 (s,1H), 8.68 (d, *J* = 1.6 Hz, 1H), 10.20 (s,1H), 7.86 (d, *J* = 2.2 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.35 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.40-3.50 (m,1H), 2.37 (t, *J* = 7.4 Hz, 2H), 1.98 (t, *J* = 7.4 Hz, 2H), 1.58-1.68 (m, 2H), 1.49-1.58 (m, 2H), 1.28-1.39 (m, 4H), 1.23 (d, *J* = 6.8 Hz, 6H). **LRMS** (ESI): (calc.) 376.5; (found) 375.2 $(M-H)^-$.	3
37	24f		N1-((R)-2-((1H-Indol-3-yl)-methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm)**:10.34 (br s,1H), 8.68 (br s,1H), 7.84 (br s,1H), 7.63 (t, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 7.0 Hz, 1H), 6.80-7.45 (m, 3H), 4.19 (br s, 1H), 3.37 (br s, 2H), 2.20-2.40 (m, 2H), 1.90-2.00 (m, 2H), 1.40-1.70 (m, 4H), 1.31 (m, 4H). **LRMS** (ESI): (calc.) 463.5; (found) 462.3 $(M-H)^-$.	3

Example 38

N1-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide (Compound 26e)

Step 5: 7-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-ylcarbamoyl)heptanoic acid (Compound **25e**)

[0136] Following the procedure described in steps 1-4 (Scheme 3) for preparation of the acid **22a** to obtain **22e**. Then, following the procedure described in Example **16**, step 3 (Scheme 1) but substituting acid **22e** for acid **3a**, the title Compound **25e** was obtained in

44% yield as a white crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.99 (br s,1H), 10.38 (s, 1H), 9.60 (s, 1H), 7.18 (m,3H), 6.93 (d, J = 6.0 Hz, 1H), 6.87 (d, J = 8.5 Hz, 2H), 6.66 (d, J = 8.6 Hz, 1H), 4.65 (d, J = 15.1 Hz, 1H), 4.29 (d, J = 15.1 Hz, 1H), 3.74 (s, 3H), 3.52 (d, J = 7.0 Hz, 1H), 2.18-2.30 (m, 4H), 1.85 (m, 1H), 1.48-1.62 (m, 4H), 1.25-1.38 (m, 4H), 0.90 (d, J = 6.7 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H). LRMS (ESI): (calc.) 481.6; (found) 482.2 $(MH)^+$.

Step 6: N1-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide (Compound **26e**)

[0137] Following the procedure described in Example 1, **4a**, step 3 (Scheme 1) but substituting acid **25e** for acid **3a**, the title Compound **26e** was obtained in 27% yield as a white crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.39 (br s, 2H), 9.62 (br s, 1H), 7.18 (s, 1H), 7.14 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 6.64 (d, J = 8.6 Hz, 1H), 4.63 (d, J = 15.1 Hz, 1H), 4.26 (d, J = 15.3 Hz, 1H), 3.50 (d, J = 7.0 Hz, 1H), 3.71 (s, 3H), 2.23 (t, J = 7.2 Hz, 2H), 1.96 (t, J = 7.2 Hz, 2H), 1.78-1.88 (m, 1H), 1.44-1.62 (m, 4H), 1.19 (m, 4H), 0.85 (d, J = 6.7 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H). LRMS (ESI): (calc.) 496.6; (found) 497.4 $(MH)^+$.

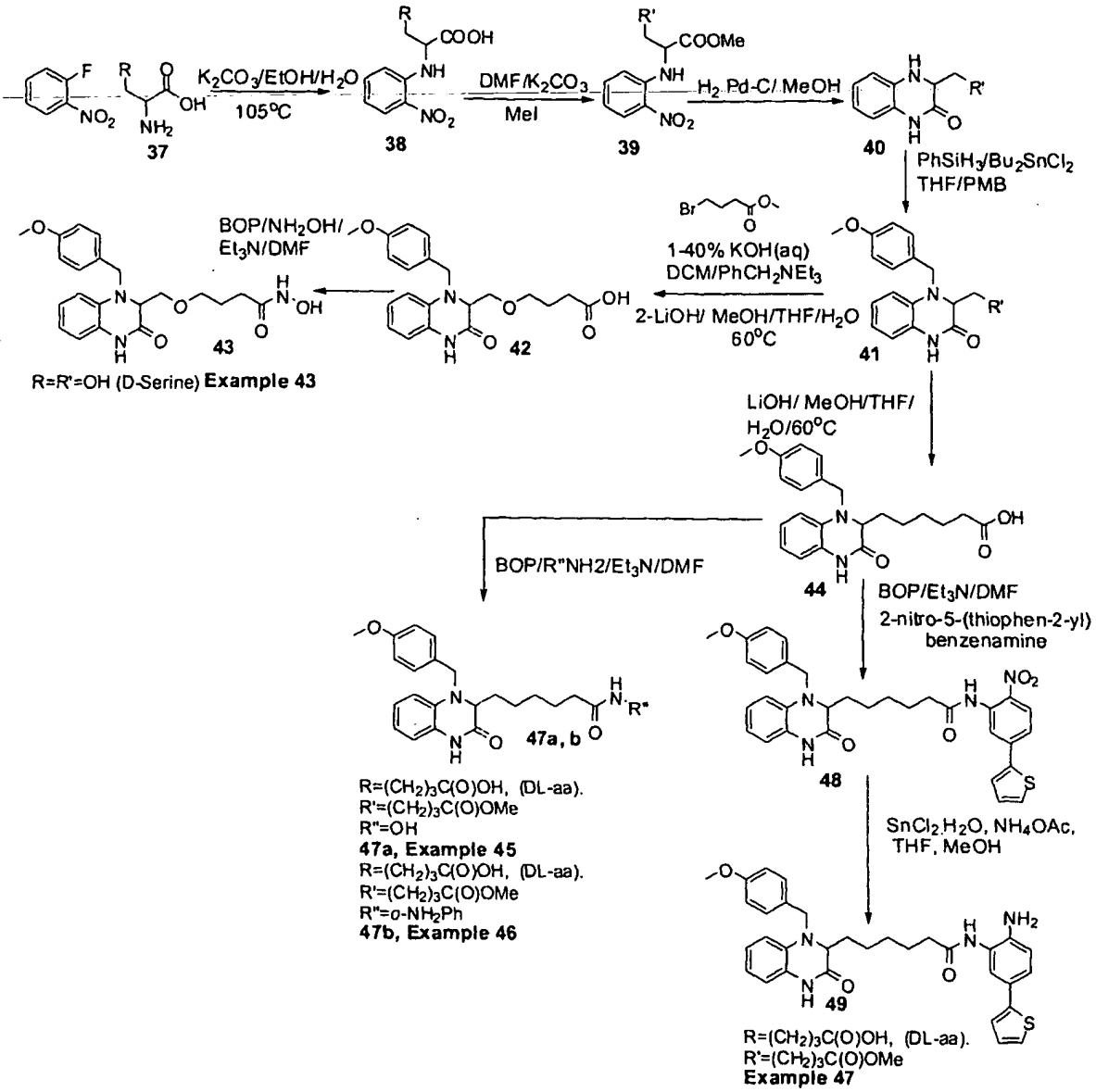
Example 40

N-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-8-(oxazol-2-yl)-8-oxooctanamide (Compound 29a)

Step 6: N-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-8-(oxazol-2-yl)-8-oxooctanamide (Compound 29a)

[0138] Following the procedure described in Example 1, Compound **4a**, step 3 (Scheme 1) and Example **39**, step 5 (Scheme 3) for preparation of amide **27a**. Oxazole (0.31 mL, 4.72 mmol) was dissolved in THF (5 mL), and the resulting solution cooled to -78°C. Butyllithium (2.95 mL, 4.72 mmol, 1.6 M solution in hexanes) was subsequently added drop wise over 15 min, followed by the addition of amide **27a** (159 mg, 0.393 mmol). The resulting solution was warmed to room temperature, and then heated to 40°C for 16 h. After cooling, the solution was diluted with aqueous ammonium chloride, and extracted with EtOAc. The organic layer was dried with Na_2SO_4, filtered, and concentrated. After purification of the residue by flash chromatography (eluent 0-100% EtOAc in hexanes), 22 mg (23%) of Compound **29a** was obtained as a light yellow crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm):10.15 (br s,1H), 7.80 (d, J = 2.2 Hz, 1H), 8.36 (s, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.50 (d, J = 1.6 Hz, 1H), 7.30 (dd, J = 8.8, 2.2 Hz, 1H), 3.63 (br s, 1H), 3.36-3.44 (m, 1H), 3.06 (br s, 1H), 3.02 (m, 2H), 2.33 (t, J = 7.4 Hz, 2H), 1.54-1.68 (m, 4H), 1.30-1.38 (m, 4H), 1.18 (d, J = 6.7 Hz, 6H). LRMS (ESI): (calc.) 412.5; (found) 411.1 $(M-H)^-$.

Scheme 5



Example 43

6-((R)-1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxy-4-oxy-hexanamide (Compound 43)

Step 1: R-2-(2-Nitrophenylamino)-3-hydroxypropanoic acid (Compound **38**)

[0139] (D)-serine **37** (2.33 g, 22.2 mmol) and 1-fluoro-2-nitrobenzene (2.34 mL, 22.2 mmol) were dissolved in EtOH:H_2O (2:1, 15 mL) at room temperature. Then K_2CO_3 (6.10 g, 44.0 mmol) was added and the solution was heated at 105°C for 16 h. After cooling the reaction, the suspension was filtered and washed with EtOH:H_2O to yield 1.16 g of orange solid (23%). LRMS (ESI): (calc.) 226; (found) 227 $(MH)^+$.

Step 2: R-Methyl 2-(2-nitrophenylamino)-3-hydroxypropanoate (Compound **39**)

[0140] Compound **38** (1.16 g) was dissolved in DMF (10 mL). Then K_2CO_3 (829 mg, 1.2 mmol) and MeI (968 uL, 15 mmol) were added to the previous solution at room temperature.

The reaction mixture was stirring for 16 h, K_2CO_3 was filtered and DMF was removed. The residue was dissolved in DCM-$CHCl_3$ and was washed with brine, dried over Na_2SO_4, filtered and concentrated. Yellow solid **39** was obtained in 84% (1.01g). LRMS (ESI): (calc.) 240.2; (found) 241.2 $(MH)^+$.

Step 3: R-3,4-Dihydro-3-(hydroxymethyl)quinoxalin-2(1H)-one (Compound **40**)

[0141] Following the procedure described in Scheme 1, step 3, Example 1, Compound **4a** but substituting Compound **2a** for Compound **39**, the title Compound **40** was obtained in 52% (389 mg). LRMS (ESI): (calc.) 178.2; (found) 179.3 $(MH)^+$.

Step 4: R-4-(4-Methoxybenzyl)-3,4-dihydro-3-(hydroxymethyl)quinoxalin-2(1H)-one (Compound **41**)

[0142] Following the procedure described in Scheme 1, step 3, and Example 16 but substituting Compound **3a** for Compound **40**, the title Compound **41** was obtained as a white solid (95%, 460 mg). ^1H NMR: (DMSO-d_6) δ (ppm): 10.37 (s, 1H), 7.20 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.73-6.68 (m, 2H), 6.58-6.53 (m, 2H), 4.60 (d, J = 15.6 Hz, 1H), 4.32 (d, J = 15.6 Hz, 1H), 3.84 (t, J = 4.4 Hz, 1H), 3.70 (s, 3H), 3.54-3.51 (m, 2H). LRMS (ESI): (calc.) 298; (found) 299 $(MH)^+$.

Step 5: 6-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-4-oxy-hexanoic acid (Compound **42**)

[0143] A mixture of Compound **41** (460 mg, 1.54mmol), benzyltriethylammonium chloride (626 mg, 2.77 mmol), methyl 4-bromobutanoate (7.2 mL, 61.4 mmol), and DCM (2 mL) was stirred at room temperature for 3 days in the presence of 40% KOH (5 mL).Then water and DCM were added. The organic phase was separated, washed with brine, dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel (AcOEt:Hexanes:1:2 to AcOEt) to give the product **42** (145 mg, 24%). ^1H NMR: (DMSO-d_6) δ (ppm): 7.30 (bs, 1H), 7.21 (d, J = 8 Hz, 2H), 6.83 ((d, J = 8.0 Hz, 2H), 6.82-6.80 (m, 1H), 6.73-6.65 (m, 2H), 4.60 (d, 15.2 Hz, 1H), 4.36 (d, J = 15.6, 1H), 3.92 (bs, 1H), 3.91-3.89 (m, 2H), 3.72 (s, 3H), 3.42 (bs, 2H), 2.05-1.96 (m, 2H), 1.70-1.65 (m, 2H). LRMS (ESI): (calc.) 384; (found) 383 $(MH)^+$.

Step 6: R-6-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxy-4-oxy-hexanamide (Compound **43**)

[0144] Following the procedure described in Scheme 1, step 3, Example 1 but substituting Compound **3a** for Compound **42**, the title Compound **43** was obtained as a beige solid (49 mg, 68%). ^1H NMR: (DMSO-d_6) δ (ppm): 7.25 (d, J = 8 Hz, 2H), 7.07 (d, J = 8 Hz, 1H), 6.85 (d, J = 8.0 Hz, 2H), 6.87-6.84 (m, 1H), 6.75-6.69 (m, 2H), 4.63 (d, 15.2 Hz, 1H), 4.37 (d, J = 15.6 Hz, 1H), 3.95 (bs, 1H), 3.86-3.80 (m, 2H), 3.72 (s, 3H), 3.48 (bs, 2H), 2.0-1.98 (m, 2H), 1.76-1.72 (m, 2H). LRMS (ESI): (calc.) 399; (found) 400 $(MH)^+$.

Example 45

6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxyhexanamide (Compound 47a)

Step 5: 6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)hexanoic acid (Compound **44**)

[0145] Following the procedure described in Scheme 1, step 4, Example 18 but substituting Compound **3a** (see Example 28, step1-4, Scheme 4 for preparation) for Compound **41**, the title Compound **44** was obtained as solid (74%, 298 mg). ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.93 (s, 1H), 10.34 (s, 1H), 7.21 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 6.74-6.79 (m, 2H), 6.61-6.67 (m, 2H), 4.53 (d, J = 7.2 Hz, 1H), 4.19 (d, J = 7.2 Hz, 1H), 3.71 (s, 3H), 3.68 (t, J = 2.0 Hz, 1H), 2.1 (t, J = 7.2 Hz, 2H), 1.33-1.50 (m, 4H), 1.15-1.23 (m, 4H). LRMS (ESI): (calc.) 382.45; (found) 383.4 $(MH)^+$.

Step 6: 6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxyhexanamide (Compound **47a**)

[0146] Following the procedure described in Scheme 1, step 3, Example 1, Compound **4a** but substituting Compound **3a** for Compound **44** (see Example 44, step1-5, Scheme 5, for preparation), the title Compound **47a** was obtained in 22% (23 mg) as a yellow solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.33 (s, 1H), 10.27 (s, 1H), 8.61 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 6.86 (d, 8.0 Hz, 2H), 6.79-6.74 (m, 2H), 6.66 -6.61 (m, 2H), 4.54 (d, J = 14.8 Hz, 1H), 4.22 (d, J = 14.8 Hz, 1H), 3.71 (bs, 4H), 1.86 (dd, J = 7.6, 8.0 Hz, 2H), 1.40-1.39 (m, 4H), 1.19-1.14 (m 4H). LRMS (ESI): (calc.) 397.4; (found) 398.4 $(MH)^+$.

Example 46

6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-aminophenyl)hexanamide (Compound 47b)

Step 6: 6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-aminophenyl)hexanamide (Compound **47b**)

[0147] Following the procedure described in Scheme 1, step 3, Example 1, Compound **4a** but substituting Compound **3a** for Compound **44** (see Example 44, step1-5, Scheme 5, for preparation) and substituting hydroxylamine for benzene-1,2-diamine, the title Compound **47b** was obtained as a yellow solid (116 mg, 94%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.34 (s, 1H), 9.03 (s, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 7.6 Hz, 1H), 6.86-6.83 (m, 3H), 6.77-6.74 (m, 2H), 6.68-6.63 (m, 3H), 6.48 (dd, J = 7.6, 7.2 Hz, 1H), 4.78 (bs, 2H), 4.54 (d, J = 14,4 Hz, 1H), 4.20 (d, J = 14.4 Hz, 1H), 3.70 (bs, 4H), 2.23 (dd, J = 7.6, 7.2 Hz, 2H), 1.52-1.49 (m, 4H), 1.23 (bs, 4H). LRMS (ESI): (calc.) 472; (found) 473.5 $(MH)^+$.

Example 47

6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)hexanamide (Compound 49)

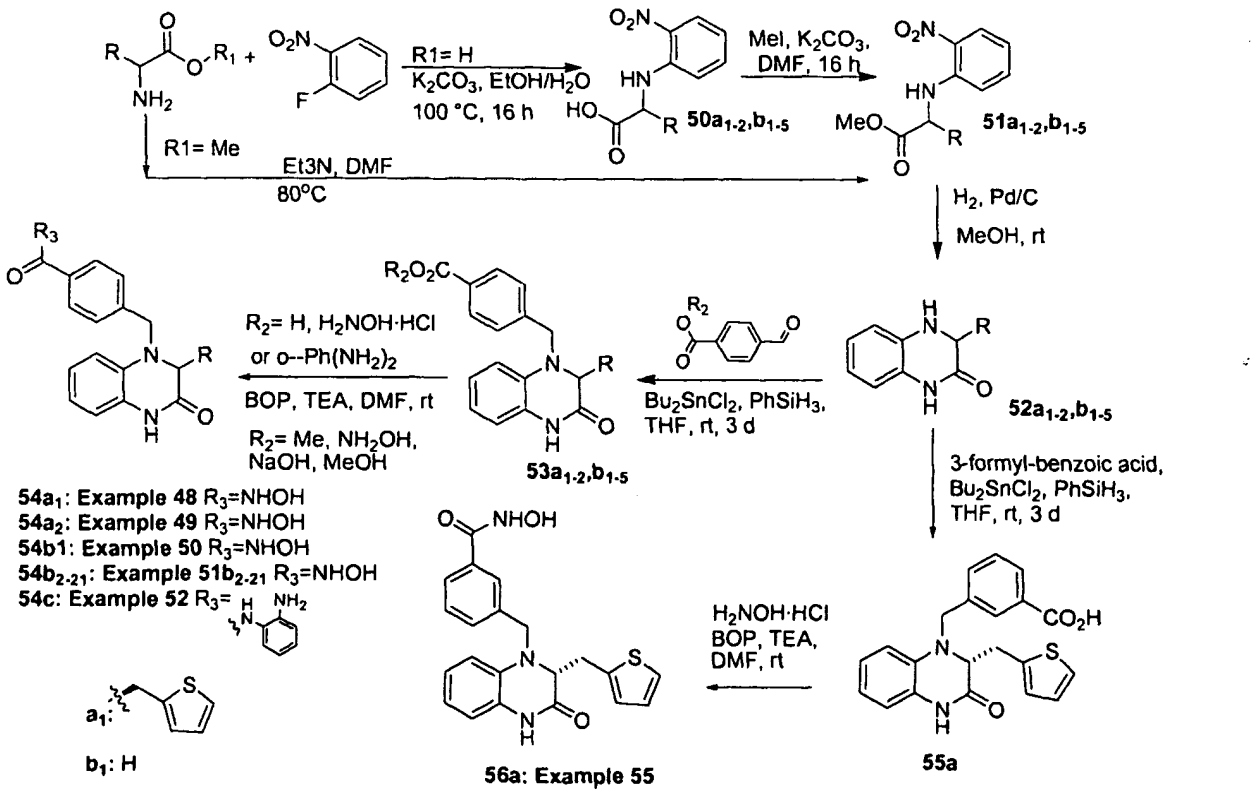
Step 6: 6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-nitro-5-(thiophen-2-yl)phenyl)hexanamide (Compound **48**)

[0148] Following the procedure described in Scheme 8, step 2, Example **62** but substituting Compound **61** for Compound **44**, and oxalyl dichloride/DCM for BOP/DMF, the title Compound was obtained in 16% (17 mg) as a solid. LRMS (ESI): (calc.) 585.1; (found) 586.2 $(MH)^+$.

Step 7: 6-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)hexanamide (Compound **49**)

[0149] Following the procedure described in Scheme 8, step 4, Example **62** but substituting Compound **62** for Compound **48**, the title Compound **49** was obtained in 99% (16 mg) as a solid. ^1H NMR: (DMSO-d_6) δ (ppm): 10.42 (s, 1H), 9.16 (s, 1H), 7.53 (s, 1H), 7.38 (d, J = 4.4 Hz, 1H), 7.28-7.24 (m, 4H), 7.08 (bs, 1H), 6.92 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.79-6.70 (m, 3H), 5.12 (bs, 1H), 4.61 (d, J = 14.8 Hz, 1H), 4.27 (d, J = 15.6 Hz, 1H), 3.70 (bs, 4H), 2.37-2.33 (m, 2H), 1.61-1.58 (m, 4H), 1.26-1.22 (m, 4H). LRMS (ESI): (calc.) 554.7; (found) 555 $(MH)^+$.

Scheme 6



Example 48

4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide (Compound $54a_1$)

Step 1: (S)-2-(2-nitrophenylamino)-3-(thiophen-2-yl)propanoic acid (Compound $50a_1$)

[0150] Both (S)-2-amino-3-(thiophen-2-yl)propanoic acid (2.51 g, 14.66 mmol) and 1-fluoro-2-nitrobenzene (1.53 mL, 14.66 mmol) were dissolved in EtOH/H_2O (5:1, 24 mL) at room temperature. Potassium carbonate (1.56 g, 11.28 mmol) was then added, and the resulting solution heated to 100°C for 16 h. After cooling, the solution was filtered, and the solvents removed. The residue, aniline **$50a_1$**, was obtained in near quantitative yield, and used in the subsequent reaction without further purification. LRMS (ESI): (calc.) 292.3; (found) 293.1 $(MH)^+$.

Step 2: (S)-Methyl 2-(2-nitrophenylamino)-3-(thiophen-2-yl)propanoate (Compound **$51a_1$**)

[0151] Aniline **$50a_1$** (4.29 g, 14.66 mmol) was dissolved in DMF (20 mL) at room temperature. Potassium carbonate (8.10 g, 58.64 mmol) and methyl iodide (2.74 mL, 43.98 mmol) were then added, and the resulting solution stirred at room temperature for 16 h. Following extraction from brine with EtOAc, the organic layer was concentrated, and the residue, aniline **$51a_1$**, was obtained in near quatitative yield. This material was used in the subsequent reaction without further purification. LRMS (ESI): (calc.) 306.3; (found) 307.2 $(MH)^+$.

Step 3: (S)-3-(Thiophen-2-ylmethyl)-3,4-dihydroquinoxalin-2(1H)-one (Compound **$52a_1$**)

[0152] Following the same procedure described in Example 1, Compound **4a,** step 2, Scheme 1, but substituting ester **$51a_1$** for acid **2a**, the title Compound was isolated in 76% yield as a light orange crystalline solid. LRMS (ESI): (calc.) 244.3; (found) 245.1 $(MH)^+$.

Step 4: 4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)benzoic acid (Compound **$53a_1$**)

[0153] Following the same procedure described in Example **16,** step 3, Scheme 1, but substituting Compound **$52a_1$** for acid **3a**, the title Compound was isolated in 81% yield as light yellow foam. LRMS (ESI): (calc.) 378.4; (found) 379.1 $(MH)^+$.

Step 5: 4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide (Compound **$54a_1$**)

[0154] Following the procedure described in Example 1, Compound **4a**, step 3 (Scheme 1) but substituting acid **$53a_1$** for acid **3a**, the title Compound was obtained in 18% yield as a light beige crystalline solid. ^1H NMR: (DMSO-d_6) δ (ppm): 11.16 (s,1H), 10.52 (s,1H), 9.02 (s, 1H), 7.67 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 5.1 Hz, 1H), 7.30 (d, J = 8.2 Hz, 2H), 6.92 (m,2H), 6.75-6.84 (m, 4H), 6.66 (t, J = 7.8 Hz, 2H), 4.64 (d, J = 15.8 Hz, 1H), 4.22 (d, J = 15.8 Hz,

1H), 4.17 (t, *J* = 6.3 Hz, 1H), 3.08 (t, *J* = 5.7 Hz, 2H). LRMS (ESI): (calc.) 393.5; (found) 394.1 $(MH)^+$.

Example 50

N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-benzamide (Compound $54b_1$)

Step 1: Methyl 2-(2-nitrophenylamino)acetate (Compound $51b_1$)

[0155] Glycine methyl ester hydrochloride (0.7534 g, 6 mmol) and 1-fluoro-3-nitrobenzene (0.8748 g, 6.2 mmol) were dissolved in DMF (6 mL). Triethylamine (2.1 mL, 15 mmol) was added to the mixture, and the reaction was heated under N_2 atmosphere, at 80°C for 16 h. The solvent was evaporated, EtOAc was added (30 mL), the organic phase was washed with water, dried over $MgSO_4$, filtered and concentrated to give crude methyl 2-(2-nitrophenylamino)acetate as an orange gum.

Step 2: 3,4-Dihydroquinoxalin-2(1H)-one (Compound $52b_1$)

[0156] Crude Compound $51b_1$ (0.932 g, 4.42 mmol) and 5% Pd/C in MeOH (25 mL) were placed under a hydrogen atmosphere (40 psi). After 1 h, the catalyst was filtered, methanol was removed and the residue was purified by flash chromatography eluting with 1:1 EtOAc/Hexanes. The title Compound $52b_1$ was obtained as a brown solid (0.325 g, 50%). ^1H NMR: (CD_3OD) δ (ppm): 8.04 (s, 1H), 6.76 (dt, J = 2.0, 7.2 Hz, 1H), 6.63 (dt, J = 1.2, 7.6 Hz, 1H), 6.61-6.57 (m, 2H), 3.87 (s, 2H), 3.75 (s, 2H). LRMS (ESI): (calc.) 148.1; (found) 149.1 $(MH)^+$.

Step 3: Methyl 4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzoate (Compound $53b_1$)

[0157] Following the procedure described in Scheme 1, step 3, and Example 16 but substituting Compound **3a** for Compound $52b_1$, the title Compound $53b_1$ was obtained as white fluffy solid (77%). ^1H NMR: (DMSO-d_6) δ (ppm): 10.43 (s, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 6.80-6.74 (m, 2H), 6.67-6.63 (m, 1H), 6.60-6.58 (m, 1H), 4.50 (s, 2H), 3.83 (s, 3H), 3.77 (s, 2H). LRMS (ESI): (calc.) 296.2; (found) 297.2 $(MH)^+$.

Step 4: N-Hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-benzamide, (Compound $54b_1$)

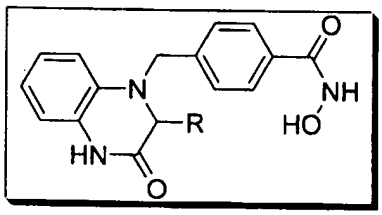
[0158] To a solution of $53b_1$ (41 mg, 0.139 mmol) in 1:1 THF/methanol (0.83 mL) was added a 50% wt solution of hydroxylamine in water (0.87 mL). Sodium hydroxide powder (44 mg, 1.112mmol) was then added to the mixture. After stirring at room temperature for 1.5 h the reaction was quenched with glacial acetic acid (0.15 mL) and then concentrated under vacuum. The product was then suspended in methanol/water (2:1) and filtered. The residue was further washed with methanol and then dried under vacuum to give the title Compound $54b_1$ as a white solid (30 mg, 73%). ^1H NMR: (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.4 (s, 1H),

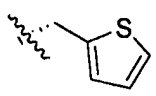
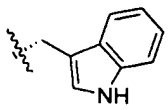
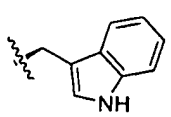
8.99 (s, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 6.89-6.75 (m, 2H), 6.67-6.62 (m, 2H), 4.46 (s, 2H), 3.75 (s, 2H). LRMS (ESI): (calc.) 297.3; (found) 298.3 $(MH)^+$.

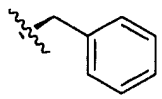
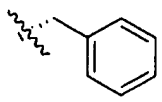
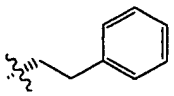
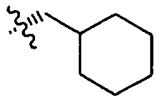
Examples 49 and 51-54

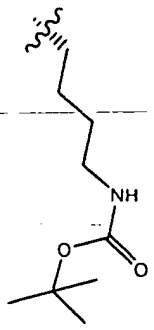
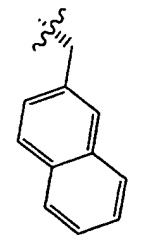
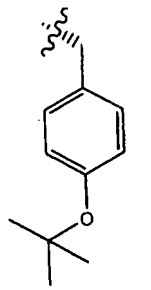
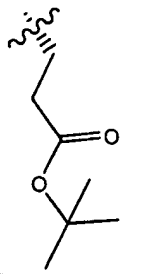
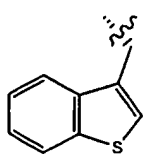
[0159] Examples 49 and 51-54 describe the preparation of Compound **54a$_2$** and **54b$_{2-21}$** using the same procedures as described for Compound **54a$_1$** in Example 48 and for Compound **54b$_1$** in Example 50. Characterization data are presented in Table 5.

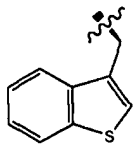
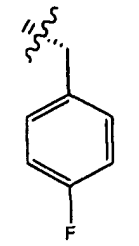
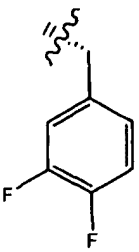
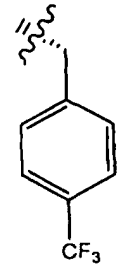
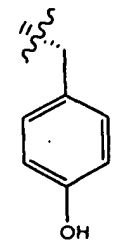
Table 5

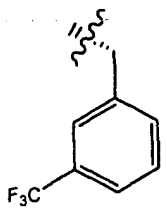
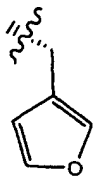
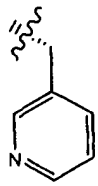


Ex	Cpd	R	Name	Characterization	Scheme
49	**54a$_2$**		4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.16 (s,1H), 10.52 (s,1H), 9.02 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 5.1 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.92 (m, 2H), 6.75-6.84 (m, 4H), 6.66 (t, *J* = 7.8 Hz, 2H), 4.64 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 4.17 (t, *J* = 6.3 Hz, 1H), 3.08 (t, *J* = 5.7 Hz, 2H). **LRMS** (ESI): (calc) 393.5; (found) 394.1 $(MH)^+$.	6
51b$_2$	**54b$_2$**		(R)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (br s, 1H), 10.8 (s, 1H), 10.4 (s, 1H), 8.97 (br s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 7.6Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.03 (t, J = 6.8 Hz, 1H), 6.99 (m, 1H), 6.92 (t, J = 6.8 Hz, 1H), 6.79-6.76 (m, 2H), 6.65 (t, J = 7.2 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 4.53 (d, J = 16.4 Hz, 1H), 4.14-4.06 (m, 2H), 2.95 (dd, J = 6.4, 14.0 Hz, 1H), 2.83 (dd, J = 6.4, 14.0 Hz, 1H). **LRMS** (ESI): (calc) 426.5; (found) 427.4 (MH^+), 449.2 (MNa^+).	6
51b$_3$	**54b$_3$**		(S)-4-((2-((1H-Indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (br s, 1H), 10.8 (s, 1H), 10.4 (s, 1H), 8.99 (br s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 7.03 (t, J = 6.8 Hz, 1H), 6.99 (m, 1H), 6.91 (t, J = 6.8 Hz, 1H), 6.79-6.76 (m, 2H), 6.65 (t, J = 7.2 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 4.53 (d, J = 16.4 Hz, 1H), 4.14-4.06 (m, 2H), 2.95 (dd, J = 6.4, 14.0 Hz, 1H), 2.83 (dd, J = 6.4, 14.0 Hz, 1H). **LRMS** (ESI): (calc) 426.5; (found) 427.2 (MH^+), 449.2 (MNa^+).	6

Ex	Cpd	R	Name	Characterization	Scheme
51b$_4$	**54b$_4$**		(S)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (CD_3OD) δ (ppm): 7.61 (d, J = 8.0 Hz, 2H), 7.24-7.16 (m, 5H), 7.08 (d, J = 7.6Hz, 2H), 6.88 (t, J = 8.0 Hz, 1H), 6.80 (d, J = 7.6 Hz, 1H), 6.73 (d, J = 7.2 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 4.49 (d, J = 15.6 Hz, 1H), 4.07 (t, J = 6.4 Hz, 1H), 3.95 (d, J = 15.6 Hz, 1H), 2.84 (d, J = 6.8 Hz, 2H). **LRMS** (ESI): (calc) 387.4; (found) 388.3 (MH^+), 410.2 (MNa^+).	6
51b$_5$	**54b$_5$**		(R)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (CD_3OD) δ (ppm): 7.60 (d, J = 8.4 Hz, 2H), 7.20-7.16 (m, 5H), 7.08 (d, J = 8Hz, 2H), 6.89 (dt, J = 1.2, 8.0 Hz, 1H), 6.80 (dd, J = 1.2, 7.6 Hz, 1H), 6.73 (dt, J = 1.2, 7.6 Hz, 1H), 6.67 (d, J = 8 Hz, 1H), 4.49 (d, J = 15.6 Hz, 1H), 4.07 (t, J = 6.4 Hz, 1H), 3.96 (d, J = 15. 6Hz, 1H), 2.83 (d, J = 6.8 Hz, 2H). **LRMS** (ESI): (calc) 387.1; (found) 388.3 (MH^+)	6
51b$_6$	**54b$_6$**	H	N-Hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** (DMSO-d6) δ (ppm): 11.1 (s, 1H), 10.4 (s, 1H), 8.99 (s, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 6.89-6.75 (m, 2H), 6.67-6.62 (m, 2H), 4.46 (s, 2H), 3.75 (s, 2H). **LRMS** (ESI): (calc) 297.3; (found) 298.3 (MH^+).	6
51b$_7$	**54b$_7$**		(R)-N-Hydroxy-4-((3-oxo-2-phenethyl-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** ($DMSO-d_6$) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 9.00 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 6.8 Hz, 2H), 7.14 (d, J = 7.2 Hz, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.81-6.75 (m, 2H), 6.65 (t, J = 7.6 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 4.69 (d, J = 16.0 Hz, 1H), 4.34 (d, J = 15.6 Hz, 1H), 3.82 (dd, J = 4.8, 8.0 Hz, 1H), 2.62-2.50 (m, 2H), 1.88-1.82 (m, 1H), 1.71-1.67 (m, 1H). **LRMS** (ESI): (calc) 401.2; (found) 402.2 (MH), 424.2 (MNa).	6
51b$_8$	**54b$_8$**		(R)-4-((2-(Cyclohexylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** ($DMSO-d_6$) δ (ppm): 11.1 (s, 1H), 10.4 (s, 1H), 9.00 (s, 1H), 7.67 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 6.79-6.75 (m, 2H), 6.66 (t, J = 8.4 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 4.64 (d, J = 15.2 Hz, 1H), 4.29 (d, J = 15.6 Hz, 1H), 3.78 (dd, J = 5.2, 8.8 Hz, 1H), 1.71 (m, 1H), 1.66-1.50 (m, 4H), 1.40-1.00 (m, 6H), 0.85-0.76 (m, 2H). **LRMS** (ESI): (calc) 393.2; (found) 394.4 (MH^+).	6

Ex	Cpd	R	Name	Characterization	Scheme
$51b_9$	$54b_9$		(R)-tert-Butyl 4-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)butylcarbamate	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.4 (s, 1H), 8.99 (s, 1H), 7.66 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 6.77-6.73 (m, 3H), 6.63 (t, J = 7.2 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 4.66 (d, J = 16.0 Hz, 1H), 4.37 (d, J = 15.6 Hz, 1H), 3.78 (m, 1H), 2.82 (m, 2H), 1.60-1.50 (m, 1H), 1.55-1.30 (m, 1H), 1.36 (s, 9H), 1.31-1.24 (m, 4H). **LRMS** (ESI): (calc) 468.6; (found) 491.4 (MNa^+).	6
$51b_{10}$	$54b_{10}$		(R)-N-hydroxy-4-((2-(naphthalen-2-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5(s, 1H), 8.98 (s, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.51-7.43 (m, 2H), 7.37 (t, J = 7.2Hz, 1H), 7.13 (d, J = 7.2 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.88-6.85 (m, 2H), 6.75 (t, J = 8.0 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 4.51 (d, J = 15.2 Hz, 1H), 4.12 (t, J = 8.4 Hz, 1H), 3.96 (d, J = 15.2 Hz, 1H), 3.28 (dd, J = 7.2, 13.6 Hz, 1H), 3.09 (dd, J = 6.8, 13.6 Hz, 1H). **LRMS** (ESI): (calc) 437.2; (found) 438.3 (MH^+).	6
$51b_{11}$	$54b_{11}$		(R)-4-((2-(4-tert-butoxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.4 (s, 1H), 8.98 (s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 6.73-6.69 (m, 1H), 6.64 (dd, J = 7.6, 1.6 Hz, 1H), 6.55 (t, J = 8.4 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 4.42 (d, J = 15.6 Hz, 1H), 4.17 (d, J = 16.0 Hz, 1H), 4.10 (t, J = 6.0 Hz, 1H), 2.77 (d, J = 6.0 Hz, 1H), 1.22 (s, 9H). **LRMS** (ESI): (calc) 459.2; (found) 460.2 (MH^+).	6
$51b_{12}$	$54b_{12}$		(R)-tert-Butyl 3-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)propanoate	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 8.99 (s, 1H), 7.66 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 6.78-6.75 (m, 2H), 6.66 (m, 1H), 6.58 (m, 1H), 4.70 (d, J = 15.6 Hz, 1H), 4.37 (d, J = 16.4 Hz, 1H), 3.85 (m, 1H), 2.22 (m, 2H), 1.78 (m, 1H), 1.63 (m, 1H). **LRMS** (ESI): (calc) 425.2; (found) 426.2 (MH^+).	6
$51b_{13}$	$54b_{13}$		(R)-4-((2-(Benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 9.00 (s, 1H), 7.94 (m, 1H), 7.62-7.61 (m, 3H), 7.34 (m, 3H), 7.21 (m, 2H), 6.80-6.78 (m, 2H), 6.68-6.64 (m, 2H), 4.59 (d, J = 14.8 Hz, 1H), 4.21-4.17 (m, 2H), 3.20-3.07 (m, 1H), 3.03-2.91 (m, 1H). **LRMS** (ESI): (calc) 443.1; (found) 444.2 (MH^+).	6

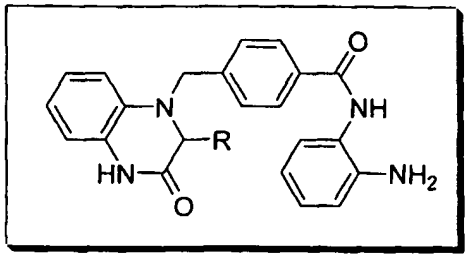
Ex	Cpd	R	Name	Characterization	Scheme
$54b_{14}$	$54b_{14}$		(S)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (br s, 1H), 10.5 (s, 1H), 9.00 (br s, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 7.59-7.57 (m, 1H), 7.34-7.29 (m, 3H), 7.20 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 7.6 Hz, 2H), 6.68 (t, J = 7.6 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 4.59 (d, J = 15.6 Hz, 1H), 4.21-4.15 (m, 2H), 3.11 (dd, J = 6.4, 14.0 Hz, 1H), 2.96 (dd, J = 7.2, 14.0 Hz, 1H). **LRMS** (ESI): (calc) 443.1; (found) 444.2(MH^+).	6
$51b_{15}$	$54b_{15}$		(R)-4-((2-(4-Fluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (br s, 1H), 10.4 (s, 1H), 8.98 (br s, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.08 (dd, J = 8.4, 5.6 Hz, 2H), 7.00 (t, J = 8.8 Hz, 2H), 6.78-6.70 (m, 2H), 6.62 (dt, J = 1.2, 7.2 Hz, 1H), 6.56 (d, J = 8.0 Hz, 1H), 4.54 (d, J = 16.0 Hz, 1H), 4.22 (d, J = 15.6 Hz, 1H), 4.10 (t, J = 6.4 Hz, 1H), 2.81 (dd, J = 6.4, 13.6 Hz, 1H), 2.75 (dd, J = 6.8, 13.6 Hz, 1H). **LRMS** (ESI): (calc) 405.15; (found) 406.2 (MH^+).	6
$54b_{16}$	$54b_{18}$		(R)-4-((2-(3,4-Difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 9.00 (br s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.22-7.13 (m, 2H), 6.89 (m, 1H), 6.74-6.70 (m, 2H), 6.62-6.55 (m, 2H), 4.60 (d, J = 15.6 Hz, 1H), 4.33 (d, J = 15.6 Hz, 1H), 4.16 (m, 1H), 2.83-2.80 (m, 2H). **LRMS** (ESI): (calc) 423.14; (found) 424.2(MH^+).	6
$51b_{17}$	$54b_{17}$		(R)-4-((2-(4-Trifluoromethylbenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 8.99 (br s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 4H), 6.76 (dt, J = 1.6, 8.4 Hz, 1H), 6.72 (dd, J = 1.6, 7.6 Hz, 1H), 6.63-6.58 (m, 2H), 4.59 (d, J = 15.6 Hz, 1H), 4.21 (d, J = 15.6 Hz, 1H), 4.16 (t, J = 6.0 Hz, 1H), 2.94 (dd, J = 6.0, 13.2 Hz, 1H), 2.82 (dd, J = 7.2, 13.2 Hz, 1H). **LRMS** (ESI): (calc) 455.2; (found) 456.2(MH^+).	6
$51b_{18}$	$54b_{18}$		(R)-N-Hydroxy-4-((2-(4-hydroxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** (CD_3OD) δ (ppm): 7.51 (m, 2H), 7.09 (m, 2H), 6.79-6.77 (m, 3H), 6.68 (m, 1H), 6.63-6.62 (m, 1H), 6.56-6.54 (m, 3H), 4.39 (d, J = 15.6 Hz, 1H), 3.89-3.84 (m, 2H), 2.65 (m, 2H). **LRMS** (ESI): (calc) 403.4; (found) 404.2 (MH^+).	6

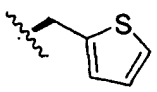
Ex	Cpd	R	Name	Characterization	Scheme
51b$_{19}$	**54b$_{19}$**		(R)-N-Hydroxy-4-((2-(3-(trifluoromethyl)benzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 8.99 (s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.40-7.35 (m, 3H), 7.29 (d, J = 8.0 Hz, 2H), 6.74 (dt, J = 1.6, 8.0 Hz, 1H), 6.68 (dd, J = 1.2, 7.2 Hz, 1H), 6.60 (dt, J = 1.2, 7.6 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 4.59 (d, J = 16.0 Hz, 1H), 4.34 (d, J = 16.0 Hz, 1H), 4.18 (t, J = 6.4 Hz, 1H), 2.95 (dd, J = 6.0, 13.6 Hz, 1H), 2.88 (dd, J = 7.6, 14.0 Hz, 1H). **LRMS** (ESI): (calc) 455.2; (found) 456.2 (MH^+).	6
51b$_{20}$	**54b$_{20}$**		(R)-4-((2-(Furan-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.1 (s, 1H), 10.5 (s, 1H), 8.99 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.44 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 6.77-6.73 (m, 2H), 6.63 (t, J = 8.0 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 6.28 (m, 1H), 6.05 (m, 1H), 4.52 (d, J = 15.6 Hz, 1H), 4.14-4.11 (m, 2H), 2.84 (dd, J = 6.4, 14.8 Hz, 1H), 2.80 (dd, J = 6.0, 14.8 Hz, 1H). **LRMS** (ESI): (calc) 377.1; (found) 378.3 (MH^+).	6
51b$_{21}$	**54b$_{21}$**		(R)-N-Hydroxy-4-((3-oxo-2-(pyridin-3-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR:** (DMSO-d_6) δ (ppm): 11.0 (s, 1H), 10.4 (s, 1H), 8.25 (d, J = 3.6 Hz, 1H), 8.16 (s, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.40 (dd, J = 6.0, 2.0 Hz, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.11 (dd, J = 4.8, 6.8 Hz, 1H), 6.68 (dt, J = 1.2, 7.6Hz, 1H), 6.62 (dd, J = 1.2, 7.6 Hz, 1H), 6.55-6.50 (m, 2H), 4.52 (d, J = 15.6 Hz, 1H), 4.24 (d, J = 16.0 Hz, 1H), 4.08 (t, J = 5.6 Hz, 1H), 2.79 (dd, J = 6.0, 13.6 Hz, 1H), 2.72 (dd, J = 7.2, 14.0 Hz, 1H). **LRMS** (ESI): (calc.) 388.2; (found) 389.2 (MH^+).	6

Example 52

[0160] Example 52 describes the preparation of Compound **54c** using the same procedures as described for Compound **54b$_1$** in Example 50. Characterization data are presented in Table 6.

Table 6



Ex	Cpd	R	Name	Characterization	Scheme
52	54c		(S)-N-(2-Aminophenyl)-4-((3-oxo-2-(thiophen-2-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.53 (s, 1H), 9.62 (s, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.40-7.33 (m, 3H), 7.15 (d, J = 7.8 Hz, 1H), 7.10-6.95 (m, 1H), 6.95-6.90 (m, 1H), 6.85-6.76 (m, 4H), 6.71-6.65 (m, 2H), 6.64-6.57 (m, 1H), 4.92 (s, 2H), 4.68 (d, J = 15.8 Hz, 1H), 4.32 (d, J = 15.6 Hz, 1H), 4.18 (t, J = 6.3 Hz, 1H), 3.15-3.04 (m, 2H) **LRMS** (ESI): (calc.) 468.6; (found) 469.2 $(MH)^+$.	6

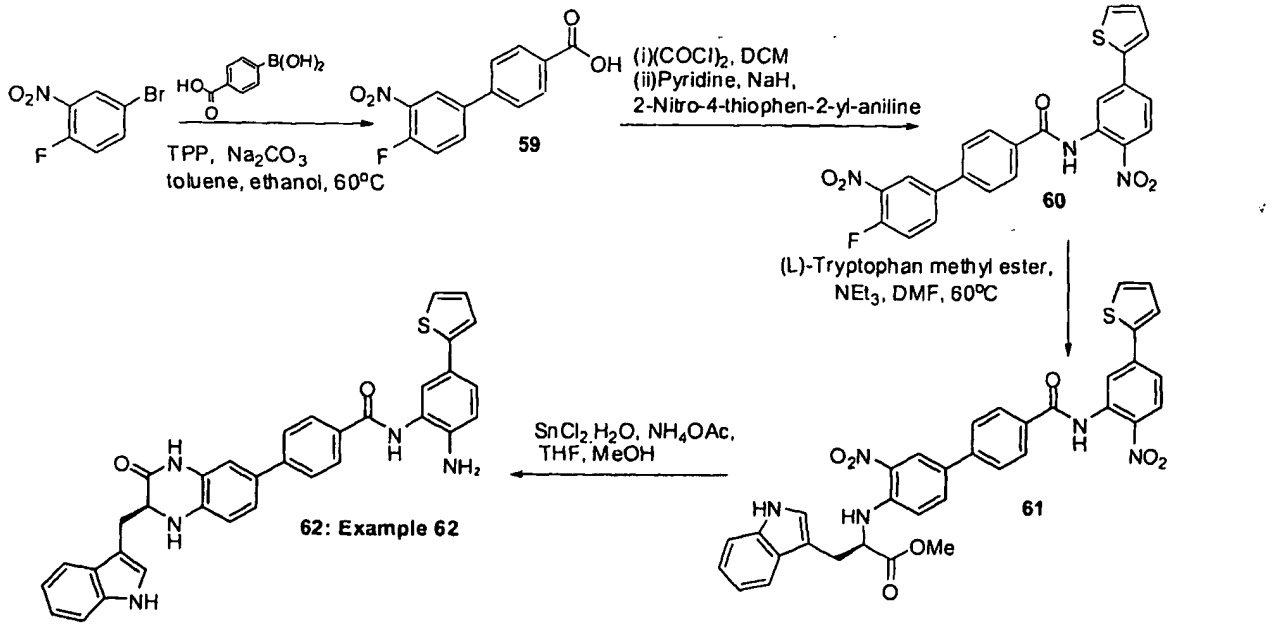
Example 55

4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide (Compound 56a)

Step 4: 4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide (Compound 56a)

[0161] Following the procedure described in Example 48, Compound **54a$_2$**, steps 1-5 (Scheme 6) but substituting (L)-2-amino-3-thiophen-2-yl-propionic acid for (D)-2-amino-3-thiophen-2-yl-propionic acid in step 1 and 3-formyl-benzoic acid for 4-formyl-benzoic acid in step 4, the title Compound was obtained in 12% yield as a light pink crystalline solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.25 (br s, 1H), 10.52 (s, 1H), 7.97 (s, 2H), 7.60-7.70 (m, 2H), 7.28-7.42 (m, 3H), 6.91 (s, 1H), 6.81 (m, 3H), 6.67 (d, J = 6.1 Hz, 2H), 4.63 (d, J = 15.3 Hz, 1H), 4.27 (d, J = 15.7 Hz, 1H), 4.19 (s, 1H), 3.09 (br s, 2H). LRMS (ESI): (calc.) 393.5; (found) 393.9 $(M-H)^-$.

Scheme 8



Example 62

4-((S)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)benzamide (Compound 62)

Step 1: p-(4-Fluro-3-nitrobenzene)-benzoic acid (Compound **59**)

[0162] To a stirred solution of 4-bromo-1-fluoro-2-nitrobenzene (2.10 g, 9.5 mmol) and 4-carboxybenzeneboronic acid (1.74 g, 10.5 mmol) in a 1:1 mixture of toluene : ethanol (40 mL), was added $Pd(PPh_3)_4$ (329 mg, 0.29 mmol), and sodium carbonate (2 M, 9.2 mL). The solution was degassed with N_2 for 5 min and then heated to 60°C and left to stir for 3 h. Water (50 mL) was added and aqueous extraction performed with EtOAc (2 x 40 mL). The organic layer was separated, dried with sodium sulfate and evaporated under reduced pressure. Purification was achieved via silica gel chromatography, employing a 1:1 AcOEt:hexanes moving to pure AcOEt solvent system. This afforded **59** as a white solid (850 mg, 35%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 8.45 (dd, J = 7.2, 2.6 Hz, 1H), 8.21-8.18 (m, 1H), 8.04 (d, J = 8.2 Hz, 2H), 7.89 (d, J = 8.2 Hz, 2H), 7.74 (dd, J = 10.0, 8.8 Hz, 1H).

Step 2 N-(2-Nitro-5-(thiophen-2-yl)4-[4-fluro-3-nitro]biphenyl)benzamide (Compound **60**)

[0163] To a stirred solution of **59** (150 mg, 0.574 mmol) in DCM (10 mL) was added oxalyl chloride (2 M, 431 mL, 0.862 mmol) and DMF (1 drop). The resulting solution was stirred for 20 min. DCM was removed via rotary evaporation and pyridine was added (10 mL), followed by 2-Nitro-4-thiophen-2-yl-aniline (126 mg, 0.574 mmol), and NaH (91 mg, 2.29 mmol). The reaction was stirred for 1 h before quenching with acetic acid (1 mL). The pyridine was removed under reduced pressure and purification was achieved through silica gel chromatography employing 4:1 AcOEt:hexanes solvent system. This afforded **60** as a yellow solid (160 mg, 60%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.23 (s, 1H), 8.52 (dd, J = 7.0, 2.6 Hz, 1H), 8.29-8.25 (m, 1H), 8.22-8.17 (m, 3H), 8.08 (d, J = 8.6 Hz, 1H), 8.00 (d, J = 8.6 Hz, 2H), 7.80-7.72 (m, 4H), 7.25 (dd, J = 5.1, 4.7 Hz, 1H).

Step 3: N-(2-Nitro-5-(thiophen-2-yl)4-[4-(S)-methyl 2-(2-nitrophenylamino)-3-(1H-indol-3-yl)propanoate-3-nitro]biphenyl)benzamide (Compound **61**)

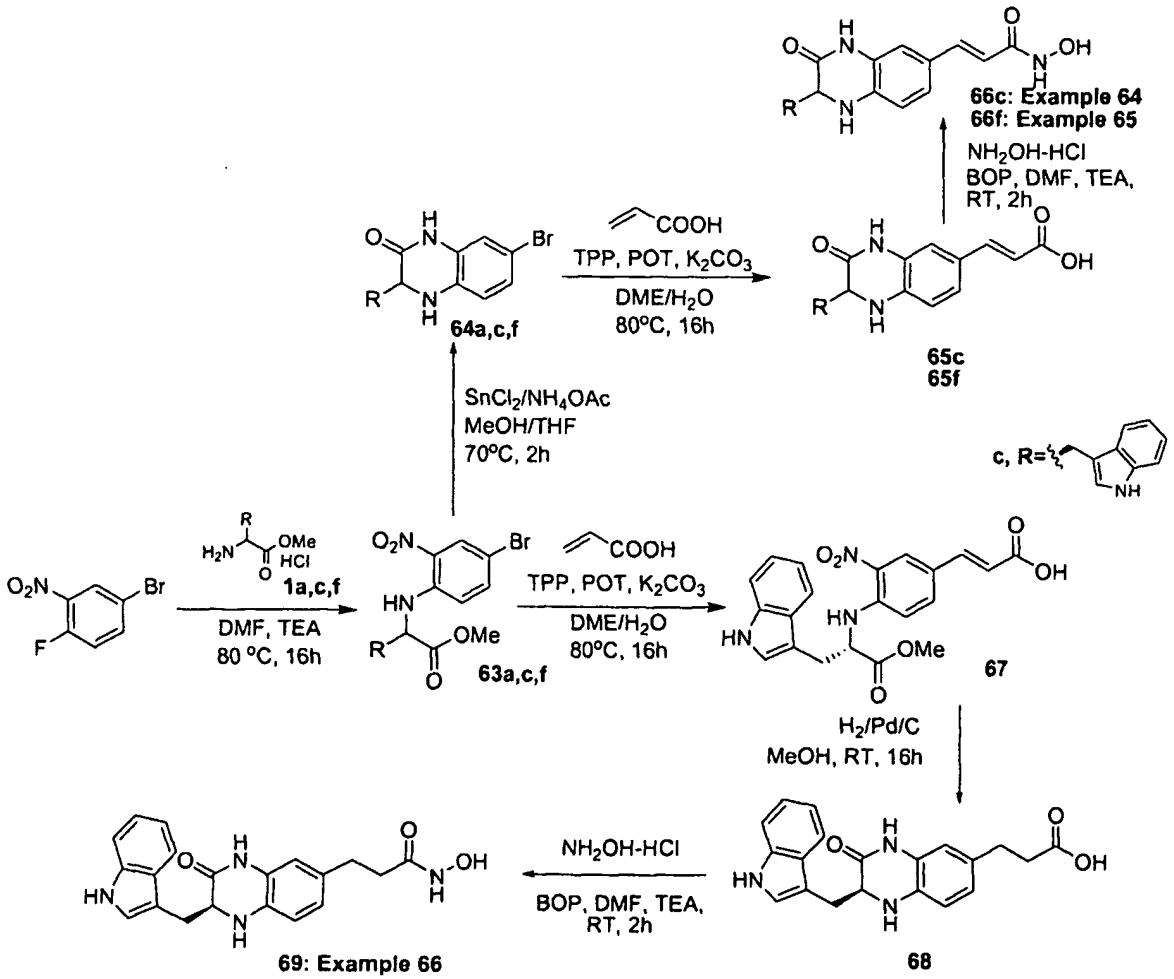
[0164] To a stirred solution of **60** (145 mg, 0.31 mmol) in DMF (3 mL) was added L-tryptophan methyl ester hydrochloride (79 mg, 0.31 mmol) and triethylamine (0.11 mL, 0.78 mmol). The solution was heated to 60°C and stirred for 15 h. Water (50 mL) was added and aqueous extraction performed with EtOAc (2 x 40 mL). The organic layer was separated, dried with sodium sulfate and evaporated under reduced pressure. Purification was achieved via silica gel chromatography, employing a 1:2 AcOEt:hexanes solvent system. This afforded **61** as an orange solid (90 mg, 43%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.01 (s, 1H), 10.92 (s, 1H), 8.47 (d, J = 2.4 Hz, 1H), 8.37 (d, J = 7.8 Hz, 1H), 8.20 (d, J = 2.0 Hz, 1H), 8.11-8.02 (m, 4H), 7.92 (d, J = 8.4 Hz, 1H), 7.78-7.71 (m, 3H), 7.40-7.34 (m, 2H), 7.27-7.21 (m, 3H), 7.08

(t, J = 7.2 Hz, 1H), 6.96 (t, J = 7.2 Hz, 1H), 5.07-5.05 (m, 1H), 3.71 (s, 3H), 3.45 (t, J = 4.7 Hz, 2H).

Step 4: 4-((S)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)benzamide (Compound **62**)

[0165] A suspension of Compound **61** (70 mg, 0.106 mmol) and tin(II) chloride dihydrate (143 mg, 0.635 mmol) in a 2:3 mixture MeOH/THF (5 mL) was stirred at 75°C in a sealed tube for 1 h, diluted with EtOAc and washed with saturated aqueous solution of $NaHCO_3$, dried over Na_2SO_4 and purified by flash chromatography, eluent 20% EtOAc in DCM, to afford Compound **62** as an orange solid (25 mg, 42%). ^1H NMR: (DMSO-d_6) δ (ppm): 10.85 (s, 1H), 10.31 (s, 1H), 9.70 (s, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 7.8 Hz, 1H), 7.46 (d, J = 2.0 Hz, 1H), 7.33 (dd, J = 5.1, 1.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.28 (dd, J = 8.2, 2.2 Hz, 1H), 7.23 (dd, J = 3.5, 1.2 Hz, 1H), 7.17 (dd, J = 8.2, 2.2 Hz, 1H), 7.12 (d, J = 2.1 Hz, 1H), 7.07-7.02 (m, 3H), 6.95 (td, J = 8.0, 1.0 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.14 (s, 1H), 5.15 (s, 2H), 4.13-4.10 (m, 1H), 3.12-2.97 (m, 2H).

Scheme 9



Example 64

(E)-3-((S)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide (Compound 66c)

Step 1: Step 1: (S)-Methyl 2-(4-bromo-2-nitrophenylamino)-3-(1H-indol-3-yl)propanoate (Compound **63c**)

[0166] Following the procedure described in Example 1, Compound **4a**, step 1, Scheme 1, but substituting (L)-valine methyl ester hydrochloride with (L)-tryptophan methyl ester hydrochloride (**1c**), and 3-nitro-4-flurobenzoic acid with 4-bromo-1-fluoro-2-nitrobenzene the title Compound was recovered as a dark orange solid in near quantitative yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 8.22 (d, J = 7.6 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 7.61 (dd, J = 2.4, 9.2 Hz, 1H), 7.30 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 2.4 Hz, 1H), 7.04-6.99 (m, 2H), 6.89 (t, J = 7.4, 1H), 4.92-4.91 (m, 1H), 3.65 (s, 3H), 3.36 (t, J = 5.6 Hz, 2H).

Step 2: (S)-3-((1H-Indol-3-yl)methyl)-7-bromo-3,4-dihydroquinoxalin-2(1H)-one (Compound **64c**)

[0167] Following the procedure described in Scheme 1, step 3, and Example 16 but substituting Compound **3a** for Compound **63c**, the title Compound **64c** was obtained in 35% yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.83 (s, 1H), 10.29 (s, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 2.0 Hz, 1H), 7.02 (t, J = 7.0 Hz, 1H), 6.93 (t, J = 7.0 Hz, 1H), 6.82 (dd, J = 8.4, 2.3 Hz, 1H), 6.77 (d, J = 2.2 Hz, 1H), 6.57 (d, J = 8.3 Hz, 1H), 6.03 (s, 1H), 4.06-4.04 (m, 1H), 3.07-2.91 (m, 2H).

Step 3: (S,E)-3-(2-((1H-Indol-3-yl)methyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-6-yl)acrylic acid (Compound **65c**)

[0168] Following the procedure described in Scheme 9, step 2, and Example 66 but substituting Compound **63c** for Compound **64c**, the title Compound **65c** was obtained in 49% yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 12.01 (br s, 1H), 10.82 (s, 1H), 10.27 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 15.8 Hz, 1H), 7.28 (dt, J = 8.0, 1.0 Hz, 1H), 7.07 (d, J = 2.4 Hz, 1H), 7.04-7.00 (m, 2H), 6.93 (td, J = 7.1, 1.0 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 6.61 (d, J = 8.2 Hz, 1H), 6.48 (d, J = 1.8 Hz, 1H), 6.01 (d, J = 15.6 Hz, 1H), 4.18-4.15 (m, 1H), 3.09-2.98 (m, 2H). LRMS (ESI): (calc.) 347.1; (found) 348.1 $(MH)^+$.

Step 4: (E)-3-((S)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide (Compound **66c**)

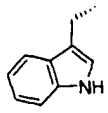
[0169] Following the procedure described in Example 1, Compound **4a**, step 3, Scheme 1, but substituting acid **3a** with acid **65c,** the title Compound was recovered with 63% yield (86 mg) (see Scheme 8, Example 43, step1-3, for preparation). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.81 (s, 1H), 10.56 (s, 1H), 10.31 (s, 1H), 8.85 (s, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 15.7 Hz, 1H), 7.07 (d, J = 2.3 Hz, 1H), 7.02 (td, J = 7.1, 1.0

Hz, 1H), 6.95-6.88 (m, 2H), 6.82 (s, 1H), 6.61 (d, J = 8.2 Hz, 1H), 6.32 (s, 1H), 6.04 (d, J = 15.7 Hz, 1H), 4.13 (m, 1H), 3.09-3.02 (m, 2H).

Example 65

[0170] Example 65 describes the preparation of Compound **66f** using the same procedures as described for Compound **66c** in Example 64. Characterization data are presented in Table 7.

Table 7

Ex.	Cpd.	R	Z	Name	Characterization	Scheme
65	66f		-NHOH	(E)-3-((R)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide	**^{1}H NMR: (CD_3OD) δ (ppm):** 7.52 (d, J = 7.8 Hz, 1H), 7.38 (d, J = 15.6 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.08-6.97 (m, 4H), 6.88-6.86 (m, 1H), 6.57 (d, J = 8.2 Hz, 1H), 6.16 (d, J = 15.6 Hz, 1H), 4.20-4.17 (m, 1H), 3.21-3.07 (m, 2H). **LRMS** (ESI): (calc.) 362.1; (found) 363.1 $(MH)^+$.	9

Example 66

3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxypropanamide (Compound 69)

Step 2: (E)-3-(4-((S)-1-(methoxycarbonyl)-2-(1H-indol-3-yl)ethylamino)-3-nitrophenyl)acrylic acid (Compound **67**)

[0171] To a stirred solution of Compound **63c** (1.35 g, 3.23 mmol) (see Example 64, step 1, Scheme 9 for preparation) in DMF (20 mL) was added $Pd_2(dba)_3$ (40 mg, 0.097 mmol), tri-*o*-toly phosphine (59 mg, 0.195 mmol), triethylamine (1.13 mL, 8.08 mmol), and acrylic acid (0.264 mL, 3.88 mmol). The resulting solution was degassed with nitrogen for 10 min and heated to 100°C for 16 h. The DMF was removed via rotary evaporation and the resulting oil was diluted with water (30 mL). Aqueous extraction was performed with EtOAc (2 x 15 mL). Purification was achieved via silica gel chromatography employing a 2:1 hexanes: EtOAc to EtOAc gradient solvent system. This afforded **63** as an orange solid (500 mg, 38%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.20 (s, 1H), 8.59 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 1.8 Hz, 1H), 7.67 (dd, J = 9.0, 1.8 Hz, 1H), 7.54 (d, J = 5.9 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.11 (s, 1H), 7.09-7.04 (m, 1H), 6.98-6.94 (m, 1H), 6.88 (d, J = 9.2 Hz, 1H), 6.32 (d, J = 5.9 Hz, 1H), 4.86-4.83 (m, 1H), 3.72 (s, 3H), 3.48-3.43 (m, 2H).

Step 3: 3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)propanoic acid (Compound **68**)

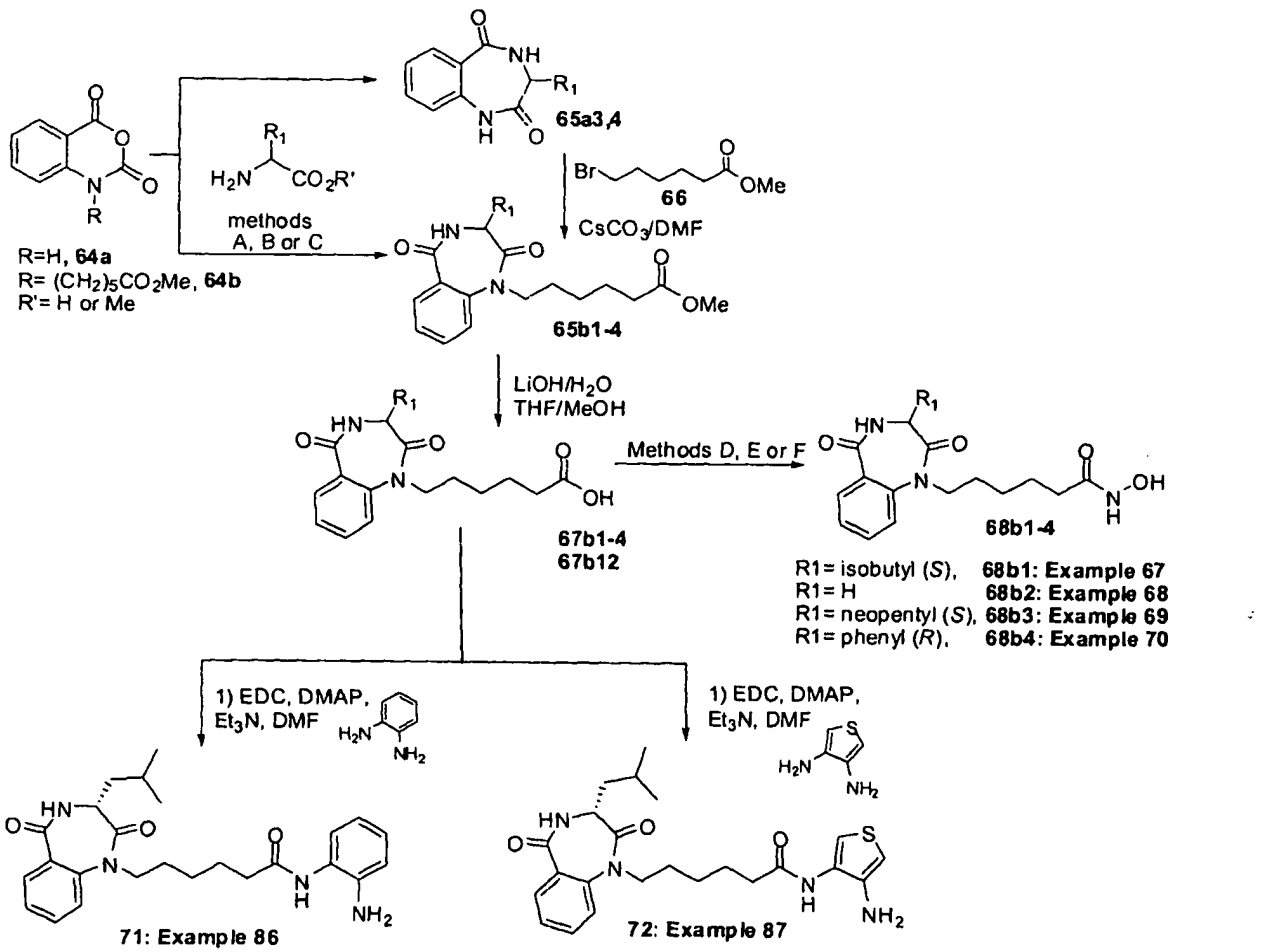
[0172] Following the procedure described in Example 1, Compound **4a**, step 2, Scheme 1 but substituting acid **2a** with acid **67**, the title Compound was recovered as a beige solid in

near 80% yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.85 (s, 1H), 10.17 (s, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.10 (s, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.95 (t, J = 7.9 Hz, 1H), 6.57-6.55 (m, 3H), 5.57 (s, 1H), 3.99-3.94 (m, 1H), 3.10-2.87 (m, 2H), 2.63 (t, J = 7.4 Hz, 2H), 2.40 (t, J = 8.0 Hz, 2H).

Step 4: 3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxypropanamide (Compound **69**)

[0173] Following the procedure described in Example 1, Compound **4a**, step 3, Scheme 1, but substituting acid **3a** with acid **68**, the title Compound was recovered as a white solid in 17% yield. ^{1}H NMR: (CD_3OD) δ (ppm): 7.52 (d, J = 7.8 Hz, 1H), 7.34-7.30 (m, 2H), 7.08 (td, J = 6.8, 1.0 Hz, 1H), 7.03-6.97 (m, 2H), 6.69 (dd, J = 8.0, 2.0 Hz, 1H), 6.61 (d, J = 1.8 Hz, 1H), 6.54 (d, J = 7.8 Hz, 1H), 4.02 (dd, J = 9.6, 3.7 Hz, 1H), 3.17 (dd, J = 14.1, 3.5 Hz, 1H), 3.00-2.94 (m, 1H), 2.79 (t, J = 7.2 Hz, 2H), 2.32 (t, J = 8.0 Hz, 2H). LRMS (ESI): (calc.) 364.1; (found) 365.1 $(MH)^+$.

Scheme 10



Synthesis of intermediate **66**: Methyl 7-bromohexanoate

[0174] To a solution 6-bromohexanoic acid (10 g, 50 mmol) in MeOH was added few drops of concentrated H_2SO_4. The mixture was then refluxed overnight. Methanol was

evaporated and the residue was taken in dichloromethane and washed with saturated solution of sodium bicarbonate and dried over $MgSO_4$. The solvent was then evaporated to give the desired ester (10.7 g) as slightly yellow oil in quantitative yield. ^1H NMR: ($CDCl_3$) δ (ppm): 3.6 (s, 3H); 3.3 (m, 2H); 2.4 (m, 2H); 1.5-1.8 (m, 4H); 1.3 (m, 2H).

Synthesis of intermediate **64b**: Methyl 6-(2,4-dioxo-2H-benzo[d][1,3]oxazin-1(4H)-yl)hexanoate

[0175] Sodium hydride (0.15 g; 6 mmol) was added to a solution of isotoic anhydride (1 g; 6 mmol) in dry DMF at 0-5°C under nitrogen. After 30 min, methyl 6-(2,4-dioxo-2H-benzo[d][1,3]oxazin-1(4H), intermediate **3** (1.26 g; 6 mmol) was added dropwise and the mixture was stirred at room temperature overnight. DMF was evaporated and the residue was taken in EtOAc and the organic layer was washed with water, brine then was dried over $MgSO_4$. The solvent was evaporated and the residue was purified on silica gel using hexanes/ EtOAc (7:3) to give **64b** (0.56 g, 32%). ^1H NMR: ($CDCl_3$) δ (ppm): 7.4 (d, J = 6 Hz, 2H); 8.2 (d, J = 6 Hz, 2H); 3.6 (s, 3H); 3.3 (m, 2H); 2.4 (m, 2H); 1.5-1.8 (m, 4H); 1.3 (m, 2H)

Example 67

6-((S)-2,3,4,5-Tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound $68b_1$)

Step 1: Formation of the benzodiazepine ring: Method A (S)-methyl 6-(3-isobutyl-2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoate (Compound **65b1**)

[0176] To a solution of isatoic anhydride **64b1** (5 mmol) (or **64a**) in acetic acid was added the L-Leucine (5 mmol) and the mixture was refluxed overnight according to the procedure of *Reddy et al. (Syn Comm. 33, 237-241, 2003)*. After cooling $NaHCO_3$ was added followed by NH_4Cl then the solution was extracted from ethyl acetate. The organic layer was washed with water and brine then dried over $MgSO_4$. After evaporation of the solvent the residue was purified on silica gel to using EtOAc to give **65b1** (or **65a**).

Step 2: (S)-6-(3-Isobutyl-2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoic acid (Compound **67b1**)

[0177] To a solution of ester **65b1** (50 mg, 0.14 mmol) in 10 mL MeOH:THF (1:1) was added a solution of lithium hydroxide (0.2 mmol) in water (5 mL). After 90 min the solvent was evaporated and the residue was acidified with HCl 1 N till pH 4 then extracted with EtOAc to give the desired acid **67b1**.

Step 3: 6-((S)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound $68b_1$). Method E

[0178] To a solution of the acid **67b1** (0.21 mmol) in DMF was added HOBt (0.21 mmol), EDCI (0.21 mmol), DMAP (0.21 mmol) and the resin bound O-Hydroxylamine (0.07 mmol, purchased commercially from NovaBiochem or prepared according to the procedure of *Floyd*

et al. Tet. Lett., 8045-8048, 1996). The mixture was shacked overnight. The resin was then washed with DMF (3x), DCM (3x) and MeOH (3x) and dried under high vaccum. This resin was treated with TFA:DCM (20%) for 4 h and the liquid was collected and evaporated to a give a residue which was purified on Prep-HPLC to give the hydroxamic acid **68b1** in 15% yield as a white solid (3 mg) after purification on prep-HPLC. ^{1}H NMR: (CD_3OD) δ (ppm): 7.8 (d, J = 8 Hz, 1H); 7.6 (d, J = 8Hz, 1H); 7.2 (m, 2H); 4.2 (m, 2H); 3.6-3.8 (m, 3H); 1.9 (dd, J = 14 Hz, 2H); 1.2-1.8(m, 6H);0.8 (2d, 6H). LRMS (ESI): (calc.) 361; (found) 362 $(MH)^+$.

Example 68

6-(2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound 68b2)

Step 1: Formation of the benzodiazepine ring: Method B Methyl 6-(2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoate (Compound **65b2**)

[0179] Following the procedure described in *J. Med. Chem.* 1999, 42, 5241, isatoic anhydride **64a** or **64b** (0.72 mmol) and the Gly-OMe methyl ester (0.80 mmol) in dry pyridine (2.0 mL) were heated at 100°C for 16 h under nitrogen. The solution was evaporated and diphenyl ether (1.5 mL) was added. The heterogeneous mixture was heated at 180°C for 1 h. Intermediate **65b2** (or **65a**) was obtained after purification on silica gel using EtOAc and hexanes. ^{1}H NMR: ($CDCl_3$) δ (ppm): 7.9 (d, J = 8 Hz, 1H); 7.6 (dd, J = 8Hz, 1H); 7.4 (dd, J = 8 Hz, 1H); 7.3 (d, J = 8Hz, 1H); 6.8 (m, 1H); 4.25 (m, 1H); 3.6-3.8 (m, 3H); 3.6 (s, 3H); 2.2 (dd, J = 14 Hz, 2H); 1.2-1.6 (m, 8H). LRMS (ESI): (calc.) 304.3; (found) 305 $(MH)^+$.

Step 2: 6-(2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoic acid (Compound **67b2**)

[0180] The title Compound **67b2** was prepared following the procedure described in Example 67, Compound **68b1**, step 2, Scheme 10, but substituting **65b1** with **65b2.** ^{1}H NMR: (CD_3OD) δ (ppm): 7.9 (d, J = 8 Hz, 1H); 7.6 (dd, J = 8Hz, 1H); 7.4 (dd, J = 8 Hz, 1H); 7.3 (d, J = 8Hz, 1H); 6.8 (m, 1H); 4.25 (m, 1H); 3.6-3.8 (m, 3H); 2.2 (dd, J = 14 Hz, 2H); 1.2-1.6 (m, 8H) LRMS (ESI): (calc.) 290.3; (found) 291 $(MH)^+$.

Step 3: 6-(2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxy-hexanamide (Compound **68b$_2$**). Method E:

[0181] Following the procedure described in Example 67, Compound **68b1**, step 3, Scheme 10, but substituting **67b1** with **67b2**, the title Compound was obtained as a white solid in 3% yield (5 mg) after purification on prep-HPLC. ^{1}H NMR: (CD_3OD) δ (ppm): 7.9 (d, J = 8 Hz, 1H); 7.6 (dd, J = 8Hz, 1H); 7.4 (dd, J = 8 Hz, 1H); 7.3 (d, J = 8Hz, 1H); 6.8 (m, 1H); 4.25 (m, 1H); 3.6-3.8 (m, 3H); 1.9 (dd, J = 14 Hz, 2H); 1.2-1.6 (m, 8H). LRMS (ESI): (calc.) 305.3; (found) 306 $(MH)^+$.

Example 69

6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound 68b3)

Step 1: Formation of the benzodiazepine ring: Method C (S)-3-neopentyl-3,4-dihydro-1H-benzo[e][1,4]diazepine-2,5-dione (**65a3**)

[0182] Following the procedure described in J. Med. Chem. 1999, 42, 5241, Isatoic anhydride **64a** (1.2 mmol) and the L-*t*-butyl leucine (1.2 mmol) in dry pyridine (4.0 mL) were heated at 115°C for 19 h under nitrogen. The solution was evaporated and diphenyl ether (4 mL) was added. The heterogeneous mixture was heated at 180°C for 3 h. Intermediate **64a3**, was obtained after purification on silica gel using EtOAc and hexanes.

Step 2: (S)-methyl 6-(3-neopentyl-2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoate (Compound 65b3).

[0183] To a solution of **64a3** (0.4 mmol) in DMF (15 mL) was added Intermediate **66** (100 mg, 0.5 mmol) followed by cesium carbonate (162 mg, 0.5 mmol). The solution was stirred for 18 h at rt. After evaporation of the solvent, the crude was purified on silica gel using EtOAc and hexanes to give the desired ester **65b3.**

Step 3: (S)-6-(3-neopentyl-2,5-dioxo-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoic acid (Compound **67b3**)

[0184] The title Compound was obtained following the procedure described in Example 67, Compound **68b1**, step 2, Scheme 10, but substituting **65b1** with **65b3.**

Step 4: 6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound **68b3**) Method D.

[0185] To a solution of the acid **67b3** (0.15 mmol) in dry DMF (5 mL) was added dry triethylamine (0.3 mmol) followed by BOP (0.22 mmol). The mixture was stirred under nitrogen at room temperature for 30 min. Then hydroxylamine hydrochloride (0.22 mmol) was added followed by triethylamine (0.3 mmol) and the mixture was stirred at room temperature for 16 h. The solvent was evaporated and the residue was purified using prep-HPLC to give the hydroxamic acid **68b3.** The title Compound **68b3** was obtained in 22% yield as white solid (29 mg) after purification by preparative TLC. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.26 (s, 1H), 8.62 (bs, 1H), 8.55 (d, J = 6.4 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 4.15 (m, 1H), 3.62 (m, 1H), 3.55 (q, J = 5.9 Hz, 1H), 2.01 (dd, J = 14.6, 5.0 Hz, 1H), 1.84 (t, J = 7.4 Hz, 2H), 1.55 (dd, J = 14.6, 6.6 Hz, 1H), 1.27-1.41 (m, 4H), 1.10 (m, 2H). LRMS (ESI): (calc.) 375.5; (found) 376.3 $(MH)^+$.

Example 70

6-((R)-2,3,4,5-Tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound 68b4)

Step 1: (R)-3-Phenyl-3,4-dihydro-1H-benzo[e][1,4]diazepine-2,5-dione (Compound **65a4**). Method B

[0186] The title Compound **65a4**, was prepared following the procedure described in Example 68, Compound **68b2**, step 1, Scheme 10, but substituting **64b** with **64a** and the L-*t*-butyl leucine with Phenyl glycine.

Step 2: (R)-methyl 6-(2,5-dioxo-3-phenyl-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoate (Compound **65b4**)

[0187] The title Compound **65b4**, was prepared following the procedure described in Example 69, Compound **68b3**, step 2, Scheme 10, but substituting **64a3** with **64a4**

Step 3: (R)-6-(2,5-Dioxo-3-phenyl-2,3,4,5-tetrahydrobenzo[e][1,4]diazepin-1-yl)hexanoic acid (Compound **67b4**)

[0188] The title Compound **67b4**, was prepared following the procedure described in Example 67, Compound **68b1**, step 2, Scheme 10, but substituting **65b1** with **65b4**.

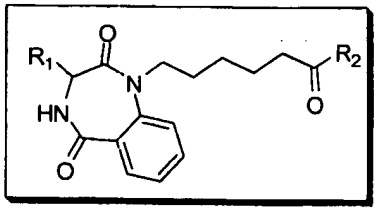
Step 4: 6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide (Compound **68b3**). Method F

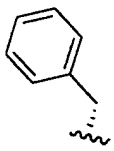
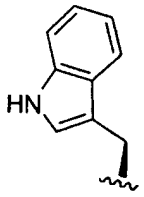
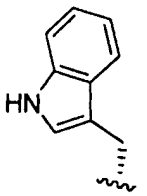
[0189] To a solution of the acid **67b4** (0.14 mmol) in THF cooled to 0°C was added triethylamine (0.19 mmol) and trimethylacetyl chloride (0.16 mmol). The resulting suspension was stirred at 0°C for 15 min. Then hydroxylamine hydrochloride (0.28 mmol) was added followed by triethylamine (0.28 mmol) and the mixture was stirred at 0°C for 15 min and at room temperature for 24 h. The solvent was evaporated and the residue was taken in ethyl acetate. The organic layer was washed with saturated solutions of ammonium chloride and then sodium bicarbonate and dried over $MgSO_4$. After concentration the residue was purified on silica gel using 5% methanol in EtOAc with 0.4% of acetic acid to give the hydroxamic acid **68b4**. The title Compound **68b4** was obtained in 11% yield as a white solid (22 mg) after purification by preparative TLC. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.28 (d, J = 5.2 Hz, 1H), 9.21 (d, J = 7.6 Hz, 0.5H), 8.89 (d, J = 6.0 Hz, 0.5H), 8.63 (s, 1H), 7.73 (dd, J = 7.6, 1.6 Hz, 0.5H), 7.64 (t, J = 7.6 Hz, 0.5H), 7.55 (d, J = 8.0 Hz, 0.5H), 7.43 (m, 1.5H), 7.37 (t, J = 7.4 Hz, 0.5H), 7.32 (m, 1.5H), 7.24 (t, J = 7.8 Hz, 0.5H), 7.12 (d, J = 8.0 Hz, 0.5H), 7.07 (t, J = 7.4 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 7.2 Hz, 1H), 5.12 (d, J = 8.0 Hz, 0.5H), 4.96 (d, J = 6.4 Hz, 0.5H), 4.18 (m, J = 7.4 Hz, 1H), 3.68 (m, 1H), 1.87 (q, J = 7.3 Hz, 2H), 1.35-1.53 (m, 4H), 1.16 (m, 2H). LRMS (ESI): (calc.) 375.5; (found) 376.3 $(MH)^+$.

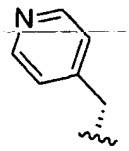
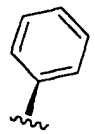
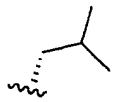
Examples 71-85 and Compound $68b_{6\text{-}12,\ 16\text{-}23_1}$

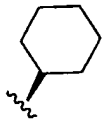
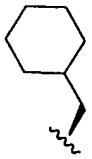
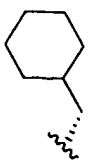
[0190] Compounds $68b_{6\text{-}12,\ 16\text{-}23_1}$, were prepared using the same procedures as described for Compound $68b_{1\text{-}4}$ in Examples 67-70. Characterization data are presented in Table 8.

Table 8



Ex	Cpd	R1/structure	R2	Name	Characterization	Scheme
71	$68b_6$		NHOH	6-((R)-2,3,4,5-Tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.8 (d, J = 8 Hz, 1H); 7.6 (d, J = 8 Hz, 1H); 7.5 (d, 7.8 Hz, 1H); 7.4 (d, J = 8Hz, 1H); 7-7.3 (m, 5H); 4.7 (t, J = 6 Hz, 1H); 3.2 (dd, J = 14 Hz, 2H); 2.8-3.2 (m, 2H); 1.9 (m, 2H); 1.2-1.8 (m, 6H). **LRMS** (ESI): (calc.) 396.4; (found) 397 $(MH)^+$.	10 Method F
72	$68b_7$		NHOH	6-((S)-3-((1H-Indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.70 (dd, J = 1.6, 7.8 Hz, 1H), 7.58 (dt, J = 1.8, 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.32 (dt, J = 1, 7.2 Hz, 1H), 7.28 (d, J = 8 Hz, 1H), 7.11 (s, 1H), 7.03 (dt, J = 1, 7 Hz, 1H), 6.90 (dt, J = 1, 7.5 Hz, 1H), 4.42 (m, 1H), 4.05 (dd, J = 6.5, 8 Hz, 1H), 3.67 (m, 1H), 3.43 (dd, J = 6, 15 Hz, 1H), 3.17 (dd, J = 7.8, 15 Hz, 1H), 1.99 (t, J = 7.4 Hz, 2H), 1.63-1.38 (m, 4H), 1.28-1.13 (m, 2). **LRMS** (ESI): (calc.) 434.5; (found) 435 $(MH)^+$.	10 Method E
73	$68b_8$		NHOH	6-((R)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.70 (dd, J = 1.6, 7.8 Hz, 1H), 7.58 (dt, J = 1.8, 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.32 (dt, J = 1, 7.2 Hz, 1H), 7.28 (d, J = 8 Hz, 1H), 7.11 (s, 1H), 7.03 (dt, J = 1, 7 Hz, 1H), 6.90 (dt, J = 1, 7.5 Hz, 1H), 4.42 (m, 1H), 4.05 (dd, J = 6.5, 8 Hz, 1H), 3.67 (m, 1H), 3.43 (dd, J = 6, 15 Hz, 1H), 3.17 (dd, J = 7.8, 15 Hz, 1H), 1.99 (t, J = 7.4 Hz, 2H), 1.63-1.38 (m, 4H), 1.28-1.13 (m, 2). **LRMS** (ESI): (calc.) 434.5; (found) 435 $(MH)^+$.	10 Method E

Ex	Cpd	R1/structure	R2	Name	Characterization	Scheme
74	68b$_9$		NHOH	6-((R)-2,3,4,5-Tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.8 (d, J = 8 Hz, 1H); 7.6 (d, J = 8 Hz, 1H); 7.5 (d, 7.8 Hz, 1H); 7.4 (d, J = 8 Hz, 1H); 7-7.3 (m, 4H); 4.7 (t, J = 6 Hz, 1H); 3.2(dd, J = 14 Hz, 2H); 2.8-3.2 (m, 2H); 1.9 (m, 2H); 1.2-1.8 (m, 6H) **LRMS** (ESI): (calc.) 396.4; (found) 397 $(MH)^+$.	10 Method E
76	68b$_{11}$		NHOH	6-((S)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.8 (m, 3H); 7.6 (m, 4H); 7.2 (m, 2H); 5.4 (m, 1H); 1.9 (dd, J = 14 Hz, 2H); 1.2-1.8 (m, 6H); **LRMS** (ESI): (calc.) 381.4; (found) 382 $(MH)^+$.	10 Method E
77	68b$_{12}$		NHOH	6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 7.78 (dd, J = 1.6, 7.8 Hz, 1H); 7.64 (dt, J = 1.8, 8.2 Hz, 1H); 7.49 (d, J = 8.4, 1H); 7.39 (dt, J = 1, 7.6 Hz, 1H), 4.39 (m, 1H), 3.75 (t, J = 8 Hz, 1H), 3.68 (m, 1H), 1.99 (t, J = 7.4 Hz, 2H), 1.74 (m, 3H), 1.62-1.38 (m, 4H), 1.3-1.1 (m, 2H), 0.92 (d, J = 6.3 Hz, 3H), 0.83 (d, J = 6.3 Hz, 3H) **LRMS** (ESI): (calc.) 361.4; (found) 362 $(MH)^+$.	10 Method E
78	68b$_{16}$		NHOH	6-(3,3-Spirocyclopentyl-2,5-dioxo-2,3,4,5,tetrahydrobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6)** δ **(ppm):** 10.27 (s, 1H), 8.62 (d, J = 5.2 Hz, 2H), 7.60 (m, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 4.15 (m, J = 7.2 Hz, 1H), 3.64 (m, 1H), 2.40 (m, 1H), 1.83 (m, 3H), 1.33-1.60 (m, 10H), 1.11 (m, 3H). **LRMS** (ESI): (calc.) 359.4; (found) 360.3 $(MH)^+$.	10 Method C & D
79	68b$_{17}$		NHOH	6-((S)-2,3,4,5-Tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4)** δ **(ppm):** 10.26 (s, 1H), 8.62 (bs, 1H), 8.55 (d, J = 6.4 Hz, 1H), 7.67 (d, J = 7.6H, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 4.15 (m, 1H), 3.62 (m, 1H), 3.55 (q, J = 5.9 Hz, 1H), 2.01 (dd, J = 14.6, 5.0 Hz, 1H), 1.84 (t, J = 7.4 Hz, 2H), 1.55 (dd, J = 14.6, 6.6 Hz, 1H), 1.27-1.41 (m, 4H), 1.10 (m, 2H).**LRMS** (ESI): (calc.) 375.5; (found) 376.3 $(MH)^+$.	10 Method C & D

Ex	Cpd	R1/structure	R2	Name	Characterization	Scheme
80	$68b_{18}$		NHOH	6-((R)-2,3,4,5-Tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 10.26 (s, 1H), 8.62 (s, 1H), 8.55 (d, J = 5.6 Hz, 1H), 7.67 (dd, J = 7.6, 1.6 Hz, 1H), 7.60 (td, J = 7.6, 1.6 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 4.15 (m, 1H), 3.62 (m, 1H), 3.55 (q, J = 5.9 Hz, 1H), 2.01 (dd, J = 14.4, 4.8 Hz, 1H), 1.84 (t, J = 7.2 Hz, 2H), 1.55 (dd, J = 14.4 6.4 Hz, 1H), 1.27-1.41 (m, 4H), 1.10 (m, 2H). **LRMS** (ESI): (calc.) 375.5; (found) 376.3 $(MH)^+$	10 Method C & D
81	$68b_{19}$		NHOH	6-((S)-3-Cyclohexyl-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (s, 1H), 8.64 (d, J = 6.8 Hz, 1H), 8.62 (s, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 4.14 (m, 1H), 3.60 (m, 1H), 3.26 (m, 1H), 1.92 (m, 1H), 1.82 (m, 3H), 1.58-1.67 (m, 3H), 1.27-1.41 (m, 4H), 1.04-1.25 (m, 6H), 0.69-0.87 (m, 2H). **LRMS** (ESI): (calc.) 387.5; (found) 388.4 $(MH)^+$.	10 Method C & D
82	$68b_{20}$		NHOH	6-((S)-3-(Cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (s, 1H), 8.62 (s, 1H), 8.55 (d, J = 5.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 4.18 (m, 1H), 3.60 (m, 2H), 1.83 (t, J = 7.4 Hz, 2H), 1.60 (m, 6H), 1.46 (m, 1H), 1.37 (m, 5H), 1.10 (m, 5H), 0.72-0.90 (m, 2H). **LRMS** (ESI): (calc.) 401.5; (found) 402.4 $(MH)^+$.	10 Method C & D
83	$68b_{21}$		NHOH	6-((R)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (s, 1H), 8.62 (s, 1H), 8.55 (d, J = 5.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 4.18 (m, 1H), 3.60 (m, 2H), 1.83 (t, J = 7.2 Hz, 2H), 1.60 (m, 6H), 1.46 (m, 1H), 1.37 (m, 5H), 1.10 (m, 5H), 0.72-0.90 (m, 2H). **LRMS** (ESI): (calc.) 401.5; (found) 402.2 $(MH)^+$.	10 Method C & D

Ex	Cpd	R1/structure	R2	Name	Characterization	Scheme
84	**68b$_{22}$**		NHOH	6-((S)-2,3,4,5-Tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.27 (bs, 1H), 8.63 (bs, 1H), 8.53 (d, J = 6.0 Hz, 1H), 7.66 (dd, J = 7.6, 1.6 Hz, 1H), 7.58 (td, J = 7.8, 1.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.31 (td, J = 7.4, 0.8 Hz, 1H), 4.18 (m, 1H), 3.77 (m, 1H), 3.61 (m, 1H), 1.84 (t, J = 7.4 Hz, 2H), 1.28-1.41 (m, 4H), 1.22 (d, J = 6.8 Hz, 3H), 1.11 (m, 2H). **LRMS** (ESI): (calc.) 319.4; (found) 320.2 $(MH)^+$.	10 Method B & D
85	**68b$_{23}$**		NHOH	6-((R)-2,3,4,5-Tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (s, 1H), 8.62 (s, 1H), 8.53 (d, J = 5.6 Hz, 1H), 7.66 (dd, J = 7.8, 1.4 Hz, 1H), 7.58 (td, J = 7.6, 1.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.31 (td, J = 7.5, 1.0 Hz, 1H), 4.18 (m, 1H), 3.77 (m, 1H), 3.61 (m, 1H), 1.84 (t, J = 7.2 Hz, 2H), 1.27-1.42 (m, 4H), 1.22 (d, J = 6.8 Hz, 3H), 1.11 (m, 2H). **LRMS** (ESI): (calc.) 319.4; (found) 320.2 $(MH)^+$.	10 Method B & F

Example 86

N-(2-Aminophenyl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide (Compound 71)

Step 3: N-(2-Aminophenyl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide (Compound **71**)

[0191] Compound **67b$_{12}$** (see Scheme 10, Example 67, step 1-2 for preparation) (40 mg, 0.12 mmol) and EDC (44 mg, 0.23 mmol), were stirred in DMF (1.5 mL) under nitrogen at room temperature for 10 min. 1,2-phenylenediamine (19 mg, 0.17 mmol) and DMAP (14 mg, 0.12 mmol) were added and the solution stirred for 16 h. The solvent was then evaporated and the residue dissolved in EtOAc. The solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, brine, and then dried over $MgSO_4$. The solvent was evaporated and the residue purified by preparative TLC (EtOAc) to give **71** as a beige solid (20 mg, 40%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 9.01 (s, 1H), 8.57 (d, J = 6.0 Hz, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.86 (t, J = 7.4 Hz, 1H), 6.68 (dd, J = 8.0, 1.2 Hz, 1H), 6.50 (t, J = 7.6 Hz, 1H), 4.79 (s, 2H), 4.20 (m, 1H), 3.56-3.67 (m, 2H), 2.21 (t, J = 7.4 Hz, 2H), 1.57-1.70 (m, 3H), 1.30-1.54 (m, 4H), 1.19 (m, 2H), 0.82 (d, J = 6.4 Hz, 3H), 0.73 (d, J = 6.4 Hz, 3H). LRMS (ESI): (calc.) 437.26; (found) 437.4 $(MH)^+$.

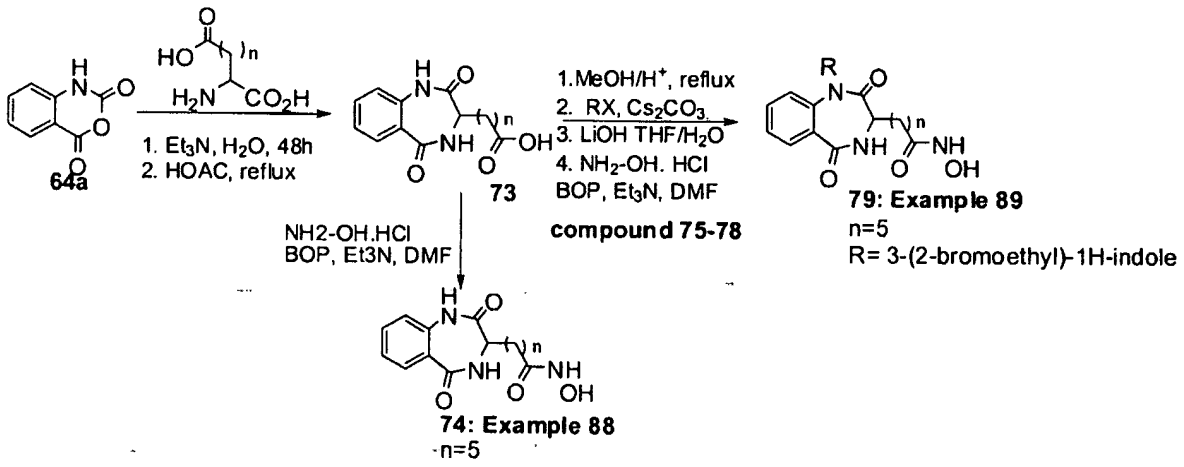
Example 87

N-(4-Aminothiophen-3-yl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide (Compound 72)

Step 3: N-(4-aminothiophen-3-yl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide (Compound 72)

[0192] Following the procedure described above (Compound 72, Example 86, Scheme 10), substituting 1,2-Phenylenediamine for 3,4-Diaminothiophene, the title Compound **72** was obtained in 29% yield as a grey solid (15 mg) after a purification on prep-HPLC. ^{1}H NMR: (DMSO-d_6) δ (ppm): 9.22 (s, 1H), 8.57 (d, J = 6.0 Hz, 1H), 7.66 (dd, J = 7.6, 1.6 Hz, 1H), 7.58 (td, J = 7.6, 1.8 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 3.6 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 6.02 (d, J = 3.6 Hz, 1H), 4.19 (m, 1H), 3.55-3.66 (m, 2H), 2.21 (t, J=7.4 Hz, 2H), 1.56-1.68 (m, 3H), 1.31-1.51 (m, 4H), 1.17 (m, 2H), 0.83 (d, J = 6.4 Hz, 3H), 0.73 (d, J = 6.4 Hz, 3H). LRMS (ESI): (calc.) 442.4; (found) 443.2 $(MH)^+$.

Scheme 11



Example 88

6-(2,3,4,5-Tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound 74)

Step 1: 6-(2,3,4,5-Tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)hexanoic acid (Compound **73**)

[0193] Isatoic anhydride **64a** (1.63 g, 10 mmol) was reacted with DL- 2-aminooctanedioic acid (1.89 g, 10 mmol) and triethylamine (2.17 g, 21.5 mmol) in H_2O (5 mL) according to the procedure of (Synthetic communications 2003, **33** (2), 237-241; Heterocyclic Chemistry 2003, **40**, 29). After 48 h at room temperature, the reaction was taken to dryness; acetic acid (10 mL) was added and the mixture was refluxed for 4h. The reaction was taken to dryness, EtOAc was added and the mixture was extracted with K_2CO_3 solution, then the aqueous layer was acidified to pH 4 with 1 N HCl and the precipitate was filtered and washed with H_2O. The title Compound was obtained in 50% yield as a grey solid

(1.45 g). ^{1}H NMR: (DMSO-d_6) δ (ppm): 12.2 (bs, 1H), 10.32 (bs, 1H), 8.42 (d, J = 5.7 Hz, 1H), 7.7 (dd, J = 1.6, 7.8 Hz, 1H), 7.47 (ddd, J = 1.8, 7.2, 7.4 Hz, 1H), 7.18 (m, 1H), 7.06 (dd, J = 1, 8.2 Hz, 1H), 3.57 (m, 1H), 2.16 (t, J = 7.2 Hz, 2H), 1.73 (m, 1H), 1.6-1.2 (m, 7H).

Step 2: 6-(2,3,4,5-Tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound **74**)

[0194] The acid **73** (180 mg, 0.62 mmol) was reacted with polymer supported hydroxyl amine 120 mg, 1.7 mmol/g) prepared according to the procedure of (European Journal of Organic Chemistry 2002, 428-438), EDC (127 mg, 0.62 mmol), HOBt (85 mg, 0.62 mmol), and DMAP (cat. amount) in DMF/ CH_2Cl_2 (5/5 mL). After 16 h at room temperature, the resin was filtered out and washed exhaustively with CH_2Cl_2, DMF, CH_2Cl_2, MeOH then CH_2Cl_2 and the resin was allowed to dry then it was treated with 20% TFA in CH_2Cl_2 (8 mL) for 1 h. The resin was filtered and washed with CH_2Cl_2 and all the filtrate was combined and concentrated leaving 55 mg of crude material. Flash chromatography with MeOH/ CH_2Cl_2 and a drop of acetic acid, gave the desired hydroxamic acid **74** as a white solid (23 mg, 12%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.25 (bs, 1H), 10.2 (bs, 1H), 8.56 (bs, 1H), 8.34 (d, J = 5.7 Hz,1H), 7.64 (dd, J = 1.6, 7.6 Hz, 1H), 7.41 (ddd, J = 1.8, 7.2, 7.4 Hz, 1H), 7.12 (dt, J= 1.2, 7.8 Hz, 1H), 7.00 (dd, J = 0.8, 8.2 Hz, 1H), 3.48 (m, 1H), 1.84 (t, J = 7.2 Hz, 2H), 1.68 (m, 2H), 1.54-1.08 (m, 7H).

Example 89

6-(1-(2-(1H-Indol-3-yl)ethyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound 79)

Step 2: Methyl 6-(2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-3-yl)hexanoate (Compound **75**)

[0195] The acid **73** (see step 1, Example 88, Scheme 11 for preparation) (100 mg, 0.34 mmol), MeOH (5 mL) and few drops of H_2SO_4 were refluxed for 10 min, the mixture was taken to dryness, and EtOAc was added and the un-reacted acid was extracted with saturated Na_2CO_3 solution. The organic layer was dried and concentrated leaving the title Compound as white solid (73 mg, 70% yield).

Step 3: Methyl 6-(1-(2-(1H-indol-3-yl)ethyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-3-yl)hexanoate (Compound **76**)

[0196] A mixture of **75** (300 mg, 0.99 mmol), 3-(2-bromoethyl)-1H-indole (242 mg, 1.1 mmol), Cs_2CO_3 (0.965 g, 3 mmol) in dry DMF (10 mL) was stirred at 40°C for 16h. H_2O was added and the product was extracted with EtOAc, and the crude product was purified by flash chromatography eluting with 20% EtOAc/hexanes. Ester **76** was obtained in 33% yield (150 mg). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.79 (s, 1H), 8.57 (d, J = 5.9 H, 1H), 7.68 (dd, J = 1.8, 7.8 Hz, 1H), 7.59 (dt, J = 1.8, 7.2 Hz, 1H), 7.51 (m, 2H), 7.31 (m, 2H), 7.03 (m, 2H), 6.95

(m, 1H), 4.33 (m, 1H), 3.91 (m, 1H), 3.59 (m, 1H), 3.55 (s, 3H), 2.81 (m, 2H), 2.27 (t, J = 7.2 Hz, 2H), 1.77 (m, 1H), 1.65 (m, 1H), 1.5 (m, 2H), 1.38-1.2 (m, 4H).

Step 4: 6-(1-(2-(1H-indol-3-yl)ethyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-3-yl)hexanoic acid (Compound **77**)

[0197] The ester methyl **76** (150 mg, 0.34 mmol), was hydrolyzed with LiOH (38 mg, 1.67 mmol) in THF/MeOH/H_2O (1:1:1 mL). After 2 h at room temperature the pH was adjusted to 3 with HCl, the mixture was taken to dryness, then, H_2O was added and the product was extracted with EtOAc, and the organic layer was concentrated giving the title Compound in 88% yield as white solid (130 mg). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.79 (s, 1H), 8.56 (d, J = 6.1 Hz, 1H), 7.68 (dd, J = 1.6, 7.6, 1H), 7.58 (dt, J = 1.8, 8.4 Hz, 1H), 7.51 (m, 2H), 7.3 (m, 2H), 7.03 (m, 2H), 6.94 (m, 1H). 4.31 (m, 1H), 3.91 (m, 1H), 3.85 (m, 2H), 2.81 (m, 2H), 2.16 (t, J = 7.2 Hz, 2H), 1.76 (m, 1H), 1.63 (m, 1H), 1.46 (m, 2H, 1.35-1.2 (m, 4H).

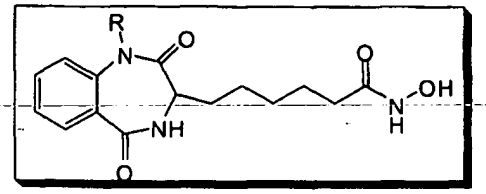
Step 5: 6-(1-(2-(1H-Indol-3-yl)ethyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound **79**)

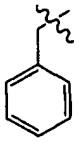
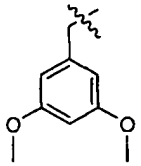
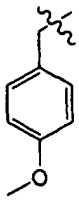
[0198] Acid **77** (110 mg, 0.25 mmol) was converted to the hydroxamic acid **79** in 1% yield as a beige solid using the procedure described in Example 88, step 2, Scheme 11. ^{1}H NMR: (CD_3OD) δ (ppm): 7.67 (dd, J = 1.6, 7.8 Hz, 1H), 7.45 (dt, J = 1.8, 8.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.18 (d, J = 8 Hz, 1H), 6.96 (dt, J = 1.2, 6.8 HZ, 1H), 6.87 (t, J = 7.8 Hz, 1H), 6.83 (s, 1H), 4.48 (m, 1H), 3.92 (m, 1H), 3.62 (t, J = 6.6 Hz, 1H), 2.87 (m, 2H), 2.0 (t, J = 7.2 Hz, 2H), 1.85 (m, 1H), 1.67 (m, 1H), 1.55 (m, 2H), 1.28 (m, 4H).

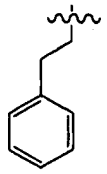
Examples 90-93

[0199] Examples 90-93 describe the preparation of Compound **80-83** using the same procedures as described for Compound **79** in Example 89, step 1-4 and Example 69, step 4 (method D), Scheme 10. Characterization data are presented in Table 9.

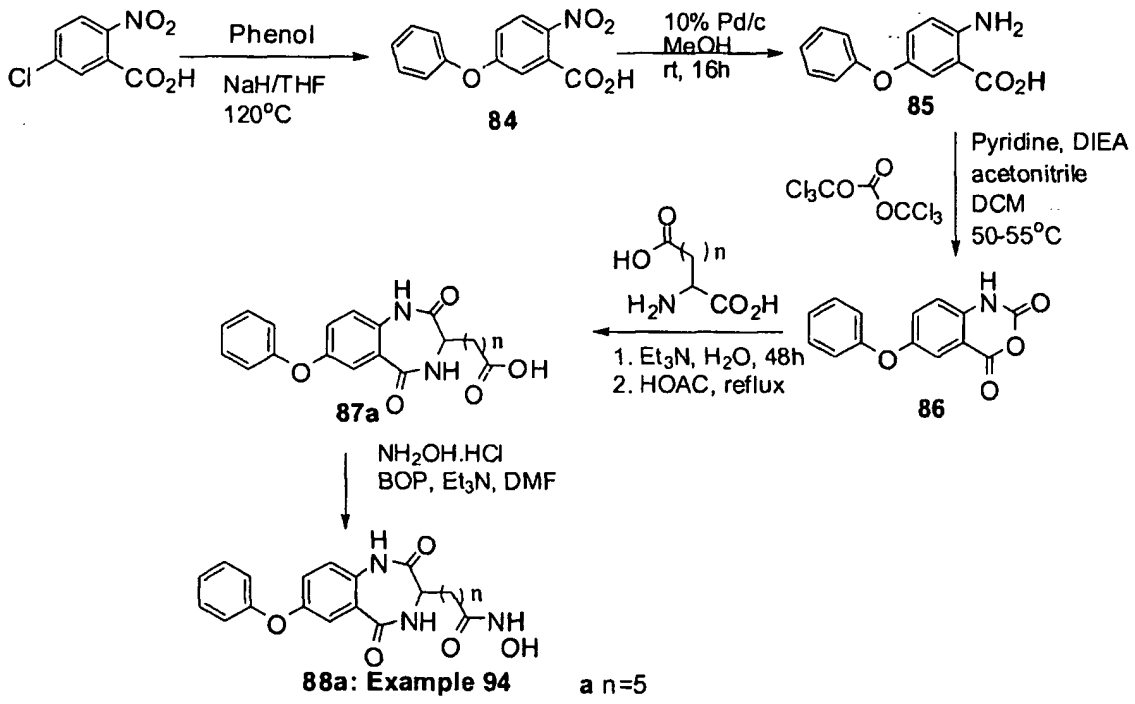
Table 9



Ex	Cpd	R	Name	Characterization	Scheme
90	80		6-(1-Benzyl-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (d, J = 1.8 Hz, 1H), 8.63 (d, J = 1.8 Hz, 1H); 8.62 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 7.6, 1.6 Hz, 1H), 7.50 (dt, 1.6, 7 Hz, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.20 (m, 4H), 7.06 (dd, J = 8.2, 1.4 Hz, 1H), 5.30 (d, J = 16 Hz, 1H), 4.96 (d, J = 16Hz, 1H), 3.69 (q, J = 6.3 Hz, 1H), 1.9 (t, J = 7, 2H), 1.76 (m, 1H), 1.65 (m, 1H), 1.5-1.2 (m, 6H). **LRMS** (ESI): (calc.) 395.5; (found) 396 $(MH)^+$.	11
91	81		6-(1-(3,5-Dimethoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.25 (s, 1H), 8.67 (d, J = 6.1Hz, 1H), 8.62 (d, J = 1.6 Hz), 7.61 (dd, J = 1.4, 7.8 Hz, 1H), 7.47 (m, 2H), 7.25 (t, J = 7.6 Hz, 1H), 6.24 (d, J = 2.1 Hz, 1H), 6.18 (d, J = 2.1 Hz, 2H), 5.3 (d, J = 16 Hz, 1H), 4.85 (d, J = 16 Hz, 1H), 3.71 (m, 1H), 3.62 (s, 6H), 1.9 (t, J = 7 Hz, 2H), 1.77 (m, 1H), 1.65 (m, 1H), 1.5-1.12 (m, 6H). **LRMS** (ESI): (calc.) 455.5; (found) 456 $(MH)^+$.	11
92	82		6-(1-(4-Methoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.58 (dd, J = 1.4, 7.6 Hz, 1H), 7.41 (m, 2H), 7.19 (m, 1H), 6.9 (d, J = 8.8 Hz, 2H), 6.63 (d, J = 8.8 Hz, 2H), 5.31 (d, J = 15.1 Hz, 1H), 4.72 (d, J = 15.1 Hz, 1H), 3.67 (dd, J = 6.5 Hz, 1H), 3.59 (s, 3H), 1.96 (t, J = 6.1 Hz, 2H), 1.85 (m, 1H), 1.65 (m, 1H), 1.5 (m, 2H), 1.34-1.18 (m, 4H). **LRMS** (ESI): (calc.) 425.5; (found) 426 $(MH)^+$.	11

Ex	Cpd	R	Name	Characterization	Scheme
93	83		6-(2,3,4,5-tetrahydro-2,5-dioxo-1-phenethyl-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 10.26 (s, 1H), 8.62 (s, 1H), 8.51(d, J = 5.5 Hz, 1H), 7.66 (d, J = 7.4 Hz, 1H), 7.57 (t, J = 7 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.22-7.08 (m, 5H), 4.31 (m, 1H), 3.88 (m, 1H), 3.53 (m, 1H), 2.69 (m, 2H), 1.89 (t, J = 7 Hz, 2H), 1.72 (m, 1H), 1.58 (m, 1H), 1.43 (m, 2H), 1.3-1.14 (m 4H). **LRMS** (ESI): (calc.) 409.5; (found) 410 $(MH)^+$.	11

Scheme 12



Example 94

6-(2,3,4,5-Tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound 88a)

Step 1: 2-Nitro-5-phenoxybenzoic acid (Compound **84**)

[0200] NaH (4 g, 60% in oil, 100 mmol) was added portion wise to a solution of phenol (9.4 g, 100 mmol,) in dry THF (50 mL). After 1h, 5-chloro-2-nitrobenzoic acid (10 g, 50 mmol) was added and the mixture was heated in a pressure tube at 120°C for 16 h. After cooling, the mixture was acidified with 1 N HCl and the product was extracted with EtOAc. The organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was washed with hexanes to remove the mineral oil giving the title Compound **84** used crude in the next reaction.

Step 2: 2-Amino-5-phenoxybenzoic acid (Compound **85**)

[0201] The crude nitro **84** was hydrogenated at 1 atm in MeOH (200 mL) using 10% Pd/C wet catalyst (1 g). After 16 h, the catalyst was filtered through Celite and the filtrate was taken to dryness and the dark residue was treated with a 2 M solution of HCl/ether, and the mixture was stirred for 2 h. The precipitate was filtered out and washed repeatedly with ether and was allowed to air dry giving the title Compound **85** as a light beige solid HCl salt (10.92 g, 82%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 8.7 (bs), 7.34 (m, 3H), 7.15 (m, 1H), 7.08 (m, 2H), 6.94 (m, 2H).

Step 3: 6-Phenoxy-1H-benzo[d][1,3]oxazine-2,4-dione (Compound **86**)

[0202] The isatoic anhydride was prepared according to the method of Huang Jun-Min et al, (Synthetic communication 2002, 14, 2215-2226). 2-Amino-5-phenoxybenzoic acid.HCl salt **85** (500 mg, 1.88 mmol) in acetonitrile (2 mL) was treated with one eq. of DIEA (328 uL, 1.88 mmol) and the mixture was placed in a preheated oil bath at 55°C. Pyridine (304 uL, 3.76 mmol) and a solution of triphosgene (186 mg, 0.627 mmol) DCM (1 mL) were added drop wise over 1 h. After 3.5 h, heating was stopped and the mixture was left at room temperature for 48 h. The reaction was taken to dryness, H_2O added and the precipitate was filtered and washed with H_2O and was allowed to air dry then it was washed repeatedly with ether giving the title Compound **86** as a beige solid in 66% yield (320 mg). LRMS (ESI): (calc.) 255; (found) 254 $(M-H)^-$. ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.74 (s, 1H), 7.49 (dd, J = 2.5, 8.8 Hz, 1H), 7.4 (m, 2H), 7.32 (d, J = 2.5 Hz, 1H), 7.17 (m, 2H), 7.02 (d, J = 7.8 Hz, 2H).

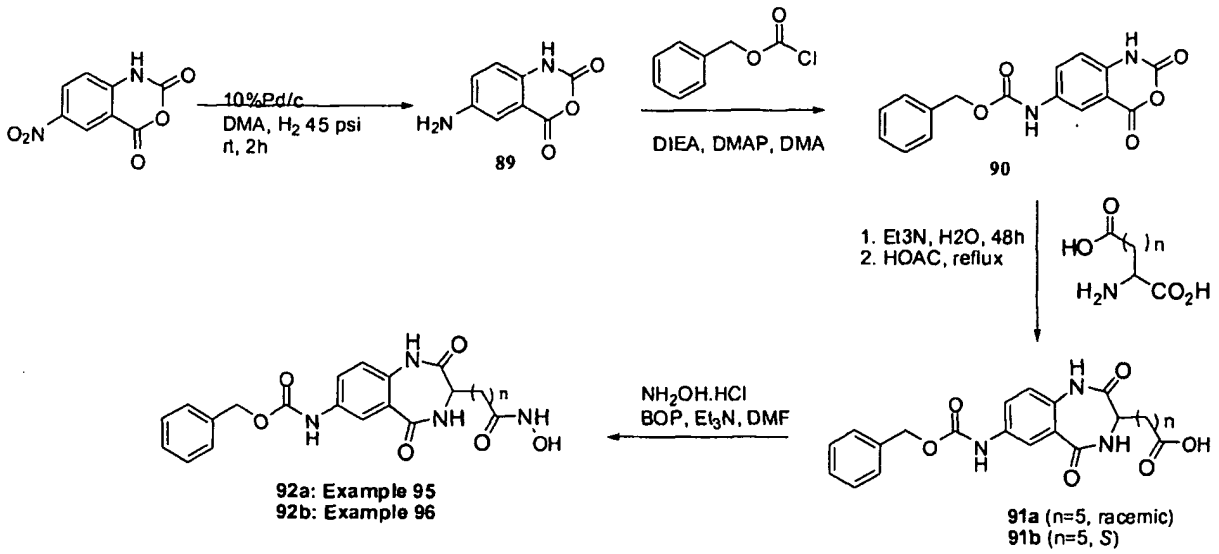
Step 4: 6-(2,3,4,5-Tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)hexanoic acid (Compound **87a**)

[0203] 6-Phenoxy-1H-benzo[d][1,3]oxazine-2,4-dione **86** (320 mg, 1.25 mmol) was reacted with DL-2-aminooctanedioic acid (237 mg, 1.25 mmol) and triethylamine (383 uL, 2.75 mmol) in H_2O (10 mL) in a manner similar to Scheme 11, step 1, Example 84. After Cyclization in acetic acid and work-up the title Compound **87a** was obtained in 25% yield as a brown solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.93 (s, 1H), 10.3 (s, 1H), 8.47 (d, J = 5.7 Hz, 1H), 7.4 (m, 2H), 7.24-7.01 (m, 6H), 3.6 (m, 1H), 2.18 (t, J = 7.2 Hz, 2H), 1.72 (m, 1H), 1.6-1.2 (m, 7H).

Step 5: 6-(2,3,4,5-Tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound **88a**)

[0204] The title Compound **88a** was obtained in 33% yield as a white solid according to method D, Scheme 10, step 4, Example 69. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.23 (s, 1H), 10.2 (s, 1H), 8.55 (s, 1H), 8.39 (d, J = 5.7 Hz, 1H), 7.32 (t, J = 8.4, 2H), 7.16-6.94 (m, 6H), 3.51 (m, 1H), 1.83 (t, J = 7.4 Hz, 2H), 1.65 (m, 1H), 1.52-1.1(m, 7H). LRMS (ESI): (calc.) 397.1; (found) 398.3.

Scheme 13



Example 95

6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound 92a)

Step 1: 6-Amino-1H-benzo[d][1,3]oxazine-2,4-dione1(Compound **89**)

[0205] 5-Nitroisatoic anhydride (500 mg, 2.4 mmol), 10% Pd/C (20 mg) in DMA (10 mL) was reduced with H_2 gas (45 psi). After 24 h, the starting material was consumed and the catalyst was filtered over a pad of Celite and crude **89** was used for the next step.

Step 2: Benzyl 2,4-dihydro-2,4-dioxo-1H-benzo[d][1,3]oxazin-6-ylcarbamate (Compound **90**)

[0206] DIEA (452 uL, 2.59 mmol) and DMAP (10 mg, 0.0816 mmol) were added to crude **89** in DMA and the mixture was cooled to -10°C in a salt-ice bath. Benzoylchloroformate (357 μL, 2.5 mmol) was added dropwise and the mix was allowed to warm-up to room temperature o/n. The solvent was removed under reduced pressure, and the crude was loaded on flash silica and eluted with 1:1 EtOAc/hex to 100% EtOAc.□The desired fractions were concentrated and the residue was triturated from minimum amount of EtOAc/ether to give the title Compound **90** as beige solid (298 mg, 40%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.61 (bs, 1H), 10.0 (bs, 1H), 8.05 (bs, 1H), 7.73 (dd, J = 8.6, 2.2 Hz, 1H), 7.36 (m, 5H), 7.08 (d, J = 8.8 Hz, 1H), 5.15 (s, 2H).

Step 3: 6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)hexanoic acid (Compound **91a**)

[0207] Compound **90** (120 mg, 0.38 mmol) was reacted with DL-2-aminooctanedioic acid (79.6 mg, 0.38 mmol) and triethylamine (115 uL, 0.83 mmol) in H_2O (1.5 mL) in a manner similar to Scheme 11, Example 88, step 1. After Cyclization in acetic acid and work-up and chromatography over flash Silica eluting with EtOAc, the title Compound **91a** was

obtained in 30% yield as a beige solid. ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.93 (bs, 1H), 10.17 (s, 1H), 9.87 (bs, 1H), 8.39 (d, J = 5.5 Hz, 1H), 7.8 (s, 1H), 7.55 (dd, J = 2, 6.5 Hz, 1H), 7.41-7.3 (m, 4H), 6.98 (d, J = 8.8 Hz, 1H), 5.13 (s, 2H), 3.53 (m, 1H), 2.16 (t, J = 7.2 Hz, 2H), 1.69 (m, 1H), 1.6-1.1 (m, 7H).

Step 4: 6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide (Compound **92a**)

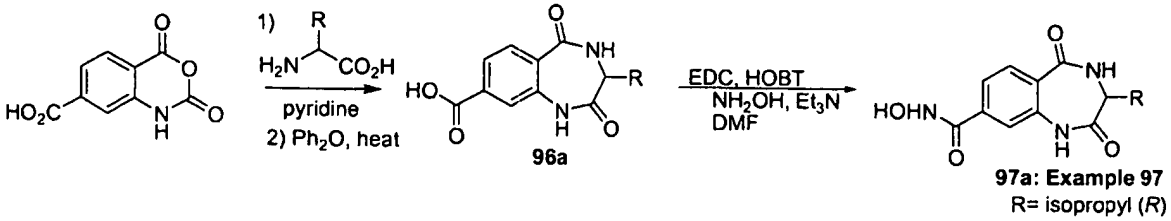
[0208] Compound **91** (38 mg, 0.087 mmol), was stirred with BOP ((42 mg, 0.095 mmol), DIEA (60.3 uL, 0.35 mmol), and hydroxyl amine hydrochloride (6.6 mg, 0.095 mmol) in DMF (2 mL) following method D, Example 69, Scheme 10, step 4. The title Compound was purified on flash Silica eluting with 75% EtOAc/hexanes with few drops of acetic acid. The fractions were combined and concentrated and the residue was triturated from acetonitrile, then from ether to remove the last traces of acetic acid. The desired hydroxamic acid **92a** was obtained as an off-white solid (17.5 mg, 44%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.26 (bs, 1H), 10.18 (s, 1H), 9.87 (s, 1H), 8.62 (bs, 1H), 8.38 (d, J = 5.9 Hz, 1H), 7.8 (d, J = 2.3 Hz, 1H), 7.55 (dd, J = 2.5, 8.8 Hz, 1H), 7.41-7.3 (m, 4H), 6.98 (d, J = 8.8 Hz, 1H), 5.13 (s, 2H), 3.52 (m, 1H), 1.9 (t, J = 7.4 Hz, 2H), 1.7 (m, 1H), 1.6-1.2 (m, 7H). LRMS (ESI): (calc.) 454.5; (found) 455.3.

Example 96

(*S*)-Benzyl 3-(6-(hydroxyamino)-6-oxohexyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-7-ylcarbamate (Compound 92b)

[0209] Following the procedure described above for Compound **92a**, the title Compound **92b** was obtained. ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.3 (s, 1H), 10.2 (s, 1H), 9.90 (s, 1H), 8.65 (s, 1H), 8.41 (d, J = 5.6 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.56 (dd, J = 2.8, 8.8 Hz, 1H), 7.42-7.32 (m, 5H), 6.99 (d, J = 8.8 Hz, 1H), 5.14 (s, 2H), 3.52 (dq, J = 2.0, 8.0 Hz, 1H), 1.89 (t, J = 7.6 Hz, 2H), 1.70 (m, 1H), 1.60-1.10 (m, 7H). LRMS (ESI): (calc.) 454.19; (found) 455.1 $(MH)^+$.

Scheme 15



97a: Example 97
R= isopropyl (*R*)

Example 97

(R)-N-Hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide (Compound 97a)

Step 1: (R)-3-Isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxylic acid (Compound **96a**)

[0210] According to the procedure of Clark et al. (Clark, A.S.; Deans, B.; Stevens, M.F.G.; Tisdale, M.J.; Whellhouse, R.T.; Denny, B.J.; Hartley, J.A. *J. Med. Chem.* **1995,** *38,* 1493-1504), 7-Carboxyisatoic anhydride (150 mg, 0.72 mmol) and D-Valine (94 mg, 0.80 mmol) in dry pyridine (2.0 mL) were heated at 100°C for 16 h under nitrogen. The solution was evaporated and phenyl ether (1.5 mL) was added. The heterogenous mixture was heated at 180°C for 1 h. The acid **96a**, was precipitated by the addition of hexane, filtered, and washed with hexane. The crude acid was dried and used without further purification.

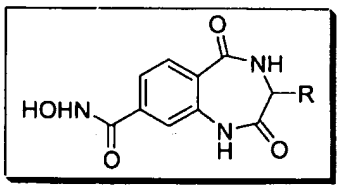
Step 2: (R)-N-Hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide (Compound **97a**)

[0211] To the acid **96a** (184 mg, 0.66 mmol) in DMF (12.1 mL) was added 1-hydroxybenzotriazole hydrate (225 mg, 1.67 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (357 mg, 1.86 mmol). The solution was stirred for 1 h at rt. Hydroxylamine hydrochloride (364 mg, 5.31 mmol) and triethylamine (0.93 mL) were added and the mixture was stirred for 16 h at rt. The solution was evaporated and the crude residue was purified by flash chromatography on silica gel, eluting with 0-20% MeOH in CH_2Cl_2. The partially purified hydroxamic acid was then purified by preparative HPLC to afford Compound **97a** (9 mg, 5% yield over three steps):

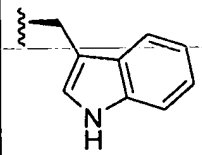
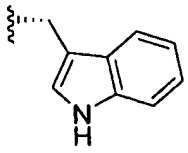
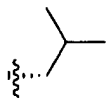
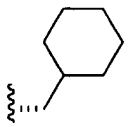
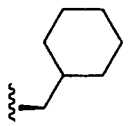
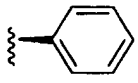
Examples 98-107

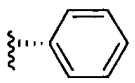
[0212] Examples 98-107 were prepared using the same procedures as described for Compound **97**, Scheme 15, Example 97. Characterization data are presented in Table 10.

Table 10

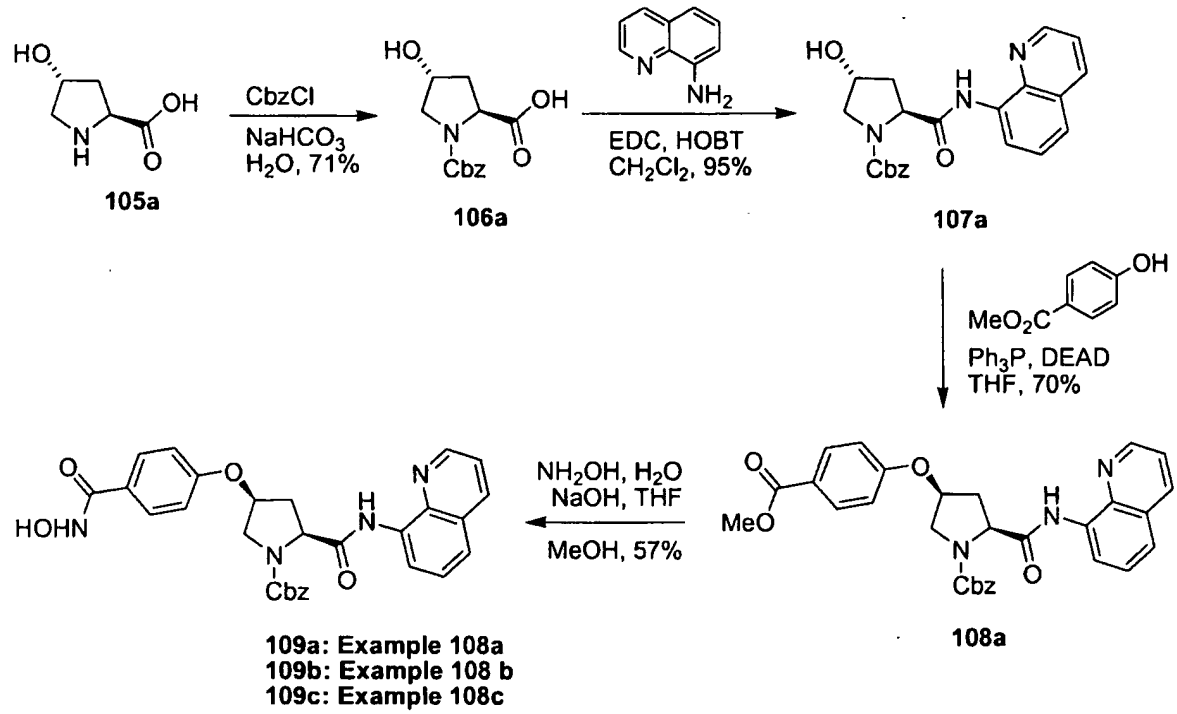


Ex	Cpd	R	Name	Characterization	Scheme
98	97b		(S)-N-Hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.29 (bs, 1H), 10.45 (s, 1H), 9.18 (bs, 1H), 8.64 (d, J = 6.5 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 3.33-3.22 (m, 1H), 1.94 (bs, 1H), 0.93 (t, J = 6.5 Hz, 3H), 0.89 (t, J = 6.5 Hz, 3H). **LRMS** (ESI): (calc.) 277.1; (found) 278.2 $(MH)^+$.	15

Ex	Cpd	R	Name	Characterization	Scheme
99	97c		(S)-3-((1H-Indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.29 (bs, 1H), 10.82 (s, 1H), 10.51 (s, 1H), 9.15 (bs, 1H), 8.51 (d, J = 5.9 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.47-7.43 (m, 3H), 7.29 (d, J = 8.0 Hz, 1H), 7.21 (s, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.87 (t, J = 7.4 Hz, 1H), 3.91-3.87 (m, 1H), 3.22 (dd, J = 14.9, 4.9 Hz, 1H), 2.98 (dd, J = 14.7, 9.4 Hz, 1H). **LRMS** (ESI): (calc.) 364.1; (found) 365.2 $(MH)^+$.	15
100	97d		(R)-3-((1H-Indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.29 (bs, 1H), 10.82 (s, 1H), 10.51 (s, 1H), 9.15 (bs, 1H), 8.51 (d, J = 5.9 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.47-7.43 (m, 3H), 7.29 (d, J = 8.0 Hz, 1H), 7.21 (s, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.87 (t, J = 7.4 Hz, 1H), 3.91-3.87 (m, 1H), 3.22 (dd, J = 14.9, 4.9 Hz, 1H), 2.98 (dd, J = 14.7, 9.4 Hz, 1H). **LRMS** (ESI): (calc.) 364.1; (found) 365.1 $(MH)^+$.	15
102	97f		(R)-N-Hydroxy-3-isobutyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.31 (bs, 1H), 10.45 (s, 1H), 9.16 (bs, 1H), 8.52 (d, J = 5.5 Hz, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.48 (d, J = 7.4 Hz, 2H), 3.61 (q, J = 6.7 Hz, 1H), 1.71-1.66 (m, 1H), 1.55 (t, J = 6.8 Hz, 2H), 0.85 (d, J = 6.5 Hz, 3H), 0.77 (d, J = 6.7 Hz, 3H). **LRMS** (ESI): (calc.) 291.1; (found) 292.1 $(MH)^+$.	15
103	97g		(R)-3-(Cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.31 (bs, 1H), 10.45 (s, 1H), 9.17 (bs, 1H), 8.51 (d, J = 5.5 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.2 Hz, 2H), 3.66 (q, J = 8.2 Hz, 1H), 1.61-1.55 (m, 7H), 1.41-1.33 (m, 1H), 1.18-1.06 (m, 3H), 0.92-0.76 (m, 2H). **LRMS** (ESI): (calc.) 331.2; (found) 332.2 $(MH)^+$.	15
104	97h		(S)-3-(Cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.31 (bs, 1H), 10.45 (s, 1H), 9.17 (bs, 1H), 8.51 (d, J = 5.5 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.2 Hz, 2H), 3.66 (q, J = 8.2 Hz, 1H), 1.61-1.55 (m, 7H), 1.41-1.33 (m, 1H), 1.18-1.06 (m, 3H), 0.92-0.76 (m, 2H). **LRMS** (ESI): (calc.) 331.2; (found) 332.1 $(MH)^+$.	15
105	97i		(S)-N-Hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.78 (d, J = 8.4 Hz, 1H), 7.40-7.38 (m, 1H), 7.38 (s, 1H), 7.25-7.18 (m, 5H), 5.13 (s, 1H). **LRMS** (ESI): (calc.) 311.1; (found) 312.2 $(MH)^+$.	15

Ex	Cpd	R	Name	Characterization	Scheme
106	97j		(R)-N-Hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (MeOD-d_4) δ (ppm):** 7.78 (d, J = 8.4 Hz, 1H), 7.40-7.38 (m, 1H), 7.38 (s, 1H), 7.25-7.18 (m, 5H), 5.13 (s, 1H). **LRMS** (ESI): (calc.) 311.1; (found) 312.2 $(MH)^+$.	15
107	97k	H	N-Hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide	**^{1}H NMR: (D_2O) δ (ppm):** 7.90 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.45 (s, 1H), 3.84 (s, 2H). **LRMS** (ESI): (calc.) 235.1; (found) 236.1 $(MH)^+$.	15

Scheme 19



109a: Example 108a
109b: Example 108 b
109c: Example 108c

Example 108a

(2S,4S)-Benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound 109a)

Step 1: (2S,4R)-1-(Benzyloxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 106a)

[0213] Sodium hydrogencarbonate (16.0 g, 191 mmol) was added to a stirred solution of *trans*-4-hydroxy-L-proline (**105a**) (10.0 g, 76 mmol) in water (8.7 mL) at 0°C. Benzyl chloroformate (12 mL, 84 mmol) was added and the mixture was stirred for 1h at 0°C, followed by 1.5h at rt. The mixture cooled to 0°C was acidified to pH 2 with concentrated HCl, and extracted with EtOAc three times. The organic layer were washed with brine, dried with $MgSO_4$, and filtered. The solution was evaporated and the crude residue was purified by flash column chromatography on silica gel, using gradient from 0-20% MeOH / CH_2Cl_2 to

afford the title Compound **106a** (14.4 g, 71% yield): LRMS (ESI): (calc.) 265.3; (found) 288.1 $(M+Na)^+$.

Step 2: (2S,4R)-benzyl 4-hydroxy-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **107a**)

[0214] 8-Aminoquinoline (681 mg, 4.73 mmol) was added to a stirred solution of Compound **106a** (835 mg, 3.15 mmol) in CH_2Cl_2 (6.8 mL). The solution was cooled to 0°C, and 1-hydroxybenzotriazole hydrate (468 mg, 3.47 mmol) was added. The mixture was stirred 5 min, then 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (665 mg, 3.47 mmol) was added. The mixture was stirred 10 min, followed by 16 h at rt. The solvent was evaporated, EtOAc and sat. aq. $NaHCO_3$ were added. The aqueous layer was extracted with EtOAc two times. The organic phases were washed with brine, dried with $MgSO_4$, and filtered. The solution was evaporated and the crude residue was purified by flash column chromatography on silica gel, using gradient from 40% to 80% EtOAc in hexane to afford the title Compound **107a** (1.18 g, 95% yield): ^1H NMR: (DMSO-d_6) δ (ppm): 10.36 (d, J = 9.6 Hz, 1H), 8.86 (bs, 1H), 8.58 (t, J = 6.4 Hz, 1H), 8.40 (d, J = 7.2 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.64-7.55 (m, 2H), 7.35-7.28 (m, 2H), 7.08 (d, J = 7.6 Hz, 1H), 6.79 (t, J = 7.2 Hz, 1H), 5.15-5.07 (m, 2H), 4.72 (dt, J = 31.2, 7.2 Hz, 1H), 4.35 (bs, 1H), 3.63-3.57 (m, 1H), 3.51 (d, J = 11.2 Hz, 1H), 2.38-2.22 (m, 1H), 2.13-2.08 (m, 1H). LRMS (ESI): (calc.) 391.2; (found) 392.2 $(MH)^+$.

Step 3: (2S,4S)-Benzyl 4-(4-(methoxycarbonyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **108a**)

[0215] Triphenylphosphine (144 mg, 0.55 mmol) was added to a stirred solution of Compound **107a** (196 mg, 0.50 mmol) in THF (5 mL) at 0°C. Methyl 4-hydroxybenzoate (80 mg, 0.53 mmol) was added, followed by diethyl azodicarboxylate (86 μL, 0.55 mmol). The mixture was allowed to warm-up to room temperature slowly and stirred 16 h at rt. The solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel, using gradient from 20% to 60% EtOAc in hexane to afford the title Compound **108a** (184 mg, 70% yield): LRMS (ESI): (calc.) 525.2; (found) 526.2 $(MH)^+$.

Step 4: (2S,4S)-Bbenzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **109a**)

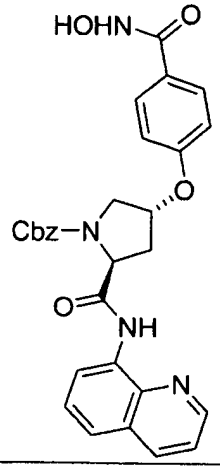
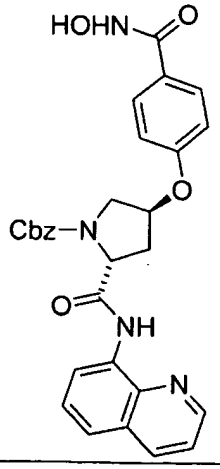
[0216] Hydroxylamine (0.5 mL, 50% in water) was added to a stirred solution of Compound **108a** (42 mg, 0.08 mmol) in THF (0.25 mL) and methanol (0.25 mL). Sodium hydroxide (26 mg, 0.64 mmol) was added, and the mixture was stirred for 1.25h. The solvent was evaporated, and the residue purified by preparative reverse phase HPLC (aquasil C-18, 100X4.6, 5uM) with MeOH/H_2O to afford the title Compound **109a** (24 mg, 57% yield). LRMS (ESI): (calc.) 526.2; (found); 527.7 $(MH)^+$. ^1H NMR: (DMSO-d_6) δ (ppm): 10.94 (bs, 1H),

10.54 (d, J = 14.5 Hz, 1H), 8.86 (s, 1H), 8.76 (d, J = 19.4 Hz, 1H), 8.60 (d, J = 7.6 Hz, 1H), 8.42 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.63-7.56 (m, 2H), 7.49 (bs, 2H), 7.39 (s, 1H), 7.30 (s, 1H), 7.09 (s, 1H), 6.90-6.83 (m, 1H), 6.68-6.64 (m, 2H), 5.27-5.21 (m, 2H), 4.74-4.61 (m, 1H), 3.97-3.78 (m, 2H), 2.78-2.68 (m, 1H), 2.50-2.33 (m, 2H).

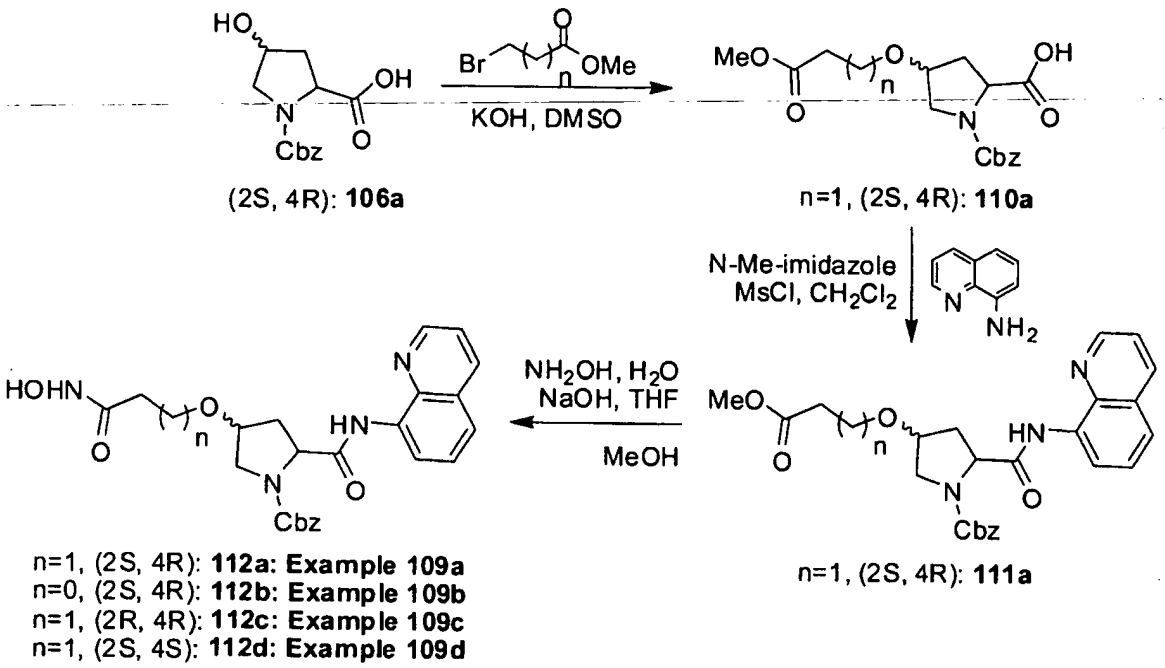
Examples 108b and 108c

[0217] Examples 108b and 108c describe the preparation of Compound **109b** and **109c** using the same procedures as described for Compound **109a** in Example 108a. Characterization data are presented in Table 11.

Table 11

Ex	Cpd	Structure	Name	Characterizaiton
108b	**109b**		(2S,4R)-Benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.08 (bs, 1H), 10.49 (s, 1H), 8.97-8.89 (m, 1H), 8.87 (d, J = 9.6 Hz, 1H), 8.61 (t, J = 6.7 Hz, 1H), 8.40 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.63-7.56 (m, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.30 (s, 2H), 7.11 (d, J = 7.3 Hz, 1H), 7.03 (d, J = 8.2 Hz, 2H), 6.81 (t, J = 7.2 Hz, 1H), 5.17 (s, 1H), 5.09 (s, 1H), 4.96-4.93 (m, 1H), 3.89-3.82 (m, 2H), 2.70-2.59 (m, 1H), 2.45-2.37 (m, 2H). **LRMS** (ESI): (calc.) 526.2; (found) 527.6 $(MH)^+$.
108c	**109c**		(2R,4S)-Benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate	**^{1}H NMR: (DMSO-d_6) δ (ppm):** 11.08 (bs, 1H), 10.49 (s, 1H), 8.97-8.89 (m, 1H), 8.87 (d, J = 9.6 Hz, 1H), 8.61 (t, J = 6.7 Hz, 1H), 8.40 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.63-7.56 (m, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.30 (s, 2H), 7.11 (d, J = 7.3 Hz, 1H), 7.03 (d, J = 8.2 Hz, 2H), 6.81 (t, J = 7.2 Hz, 1H), 5.17 (s, 1H), 5.09 (s, 1H), 4.96-4.93 (m, 1H), 3.89-3.82 (m, 2H), 2.70-2.59 (m, 1H), 2.45-2.37 (m, 2H). **LRMS** (ESI): (calc.) 526.2; (found) 527.6 $(MH)^+$.

Scheme 20



Example 109a

(2S,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound 112a)

Step 1: (2S,4R)-1-(Benzyloxycarbonyl)-4-(3-methoxy-3-oxopropoxy)pyrrolidine-2-carboxylic acid (Compound **110a**)

[0218] Potassium hydroxide (1.69 g, 30.2 mmol) was added to a stirred solution of Compound **106a** (2.00 g, 7.54 mmol) in DMSO (10 mL). Methyl 3-bromopropionate (1.65 mL, 15.1 mmol) was added dropwise to the mixture, and then stirred for 16h. Water and EtOAc were added, and concentrated HCl was added up to pH~3. The aqueous layer was extracted with EtOAc two times. The organic phases were dried with $MgSO_4$ and filtered. The solution was evaporated and the crude residue was purified by flash column chromatography on silica gel, using 60% EtOAc in hexane to afford the title Compound **110a** (376 mg, 14% yield). LRMS (ESI): (calc.) 351.1; (found); 352.3 $(MH)^+$.

Step 2: (2S,4R)-Benzyl 4-(3-methoxy-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **111a**)

[0219] 1-Methylimidazole (88 μL, 1.10 mmol) was added to a stirred solution of Compound **110** (176 mg, 0.50 mmol) in CH_2Cl_2 (2.5 mL). The solution was cooled to 0°C and methanesulfonyl chloride (39 μL, 0.50 mmol) was added drop-wise. The reaction was allowed to reach room temperature, then 8-aminoquinoline (65 mg, 0.45 mmol) was added. The mixture was stirred at 45°C for 16 h. The reaction was quenched with sat. aq. NH_4Cl, and extracted three times with CH_2Cl_2. The organic phases were dried with $MgSO_4$ and filtered. The solution was evaporated and the crude residue was purified by flash column

chromatography on silica gel, using gradient from 10% to 60% EtOAc in hexane to afford the title Compound **111a** (120 mg, 56% yield). LRMS (ESI): (calc.) 477.2; (found) 478.0 $(MH)^+$.

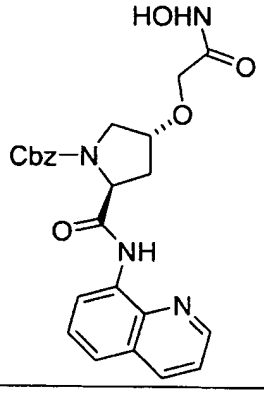
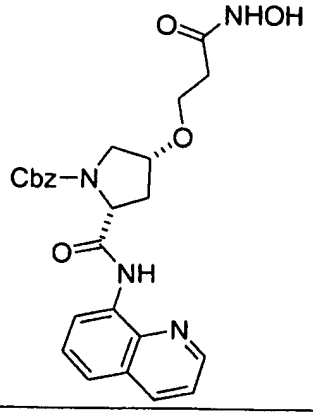
Step 3: (2S,4R)-Benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **112a**)

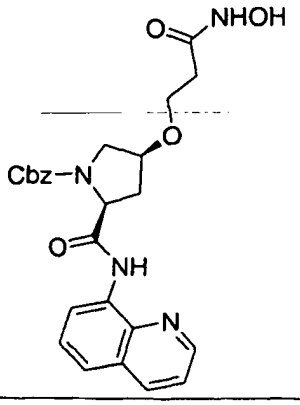
[0220] Hydroxylamine (1.1 mL, 50% in water) was added to a stirred solution of Compound **111a** (106 mg, 0.22 mmol) in THF (0.6 mL) and methanol (0.6 mL). Sodium hydroxide (89 mg, 2.2 mmol) was added, and the mixture was stirred for 1.5 h. The solvent was evaporated, and the residue purified by preparative reverse phase HPLC (aquasil C-18, 100X4.6, 5uM) with MeOH in H_2O to afford the title Compound **112a** (44 mg, 42% yield): ^1H NMR: (DMSO-d_6) δ (ppm): 10.39 (s, 1H), 8.90-8.84 (m, 1H), 8.77 (s, 1H), 8.62-8.58 (m, 1H), 8.40 (d, J = 8.0 Hz, 1H), 7.70-7.54 (m, 3H), 7.37-7.28 (m, 2H), 7.08 (d, J = 7.2 Hz, 1H), 6.78 (t, J = 7.2 Hz, 1H), 5.12-5.05 (m, 2H), 4.71 (dt, J = 29.6, 7.6 Hz, 1H), 4.15 (s, 1H), 3.70-3.56 (m, 4H), 2.21-2.10 (m, 4H). LRMS (ESI): (calc.) 478.2; (found) 479.3 $(MH)^+$.

Examples 109b, 109c and 109d

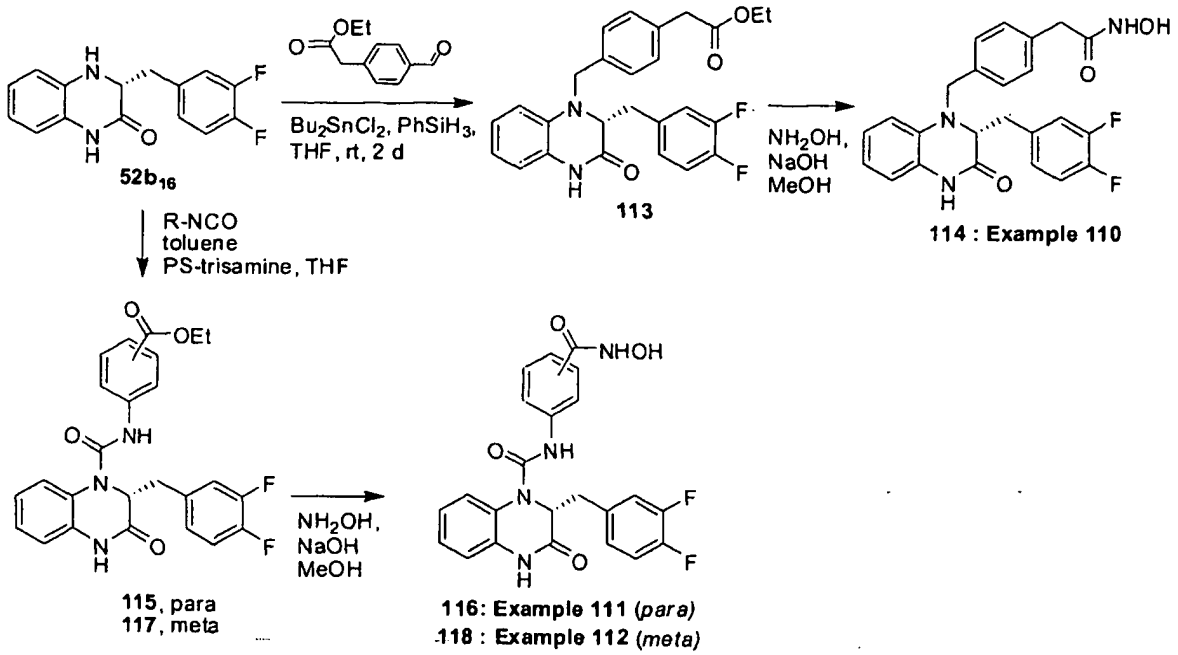
[0221] Examples 109b, 109c and 109d describe the preparation of Compound **112b**, **112c** and **112d** using the same procedure as described for Compound **112a** in Example 108a. Characterization data are presented in Table 12.

Table 12

Ex	Cpd	Structure	Name	Characterization
109b	**112b**		(2S,4R)-benzyl 4-(2-(hydroxyamino)-2-oxoethoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate	**^1H NMR: ($CDCl_3$) δ (ppm):** 10.71 (s, 1H), 8.73 (s, 1H), 8.69 (t, J=4.5 Hz, 1H), 8.18 (d, J=8.0 Hz, 1H), 7.55 (d, J=3.7 Hz, 2H), 7.45-7.41 (m, 1H), 7.30-7.24 (m, 5H), 5.08-5.00 (m, 2H), 4.69-4.64 (m, 1H), 4.38-4.32 (m, 1H), 4.22 (d, J=5.3 Hz, 2H), 3.95 (d, J=11.7 Hz, 1H), 3.63 (dd, J=11.5, 4.8 Hz, 1H), 2.68-2.58 (m, 1H), 2.57-2.43 (m, 1H). **LRMS** (ESI): (calc.) 464.2; (found) 465.2 $(MH)^+$.
109c	**112c**		(2R,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate	**^1H NMR: (DMSO-d_6) δ (ppm):** 10.45 (d, J=5.6 Hz, 1H), 10.24-10.22 (m, 1H), 8.85-8.82 (m ,1H), 8.66 (s, 1H), 8.61 (d, J=7.4 Hz, 1H), 8.39 (d, J=8.0 Hz, 1H), 7.66-7.54 (m, 3H), 7.37 (s, 1H), 7.29 (s, 1H), 7.07 (d, J=6.5 Hz, 1H), 6.83-6.78 (m, 1H), 5.23-4.94 (m, 2H), 4.54 (dd, J=26, 9.6 Hz, 1H), 4.16 (s, 1H), 3.68-3.56 (m, 5H), 2.22-2.18 (m, 1H), 2.05-1.98 (m, 2H). **LRMS** (ESI): (calc.) 478.2; (found) 479.3 $(MH)^+$.

Ex	Cpd	Structure	Name	Characterization
109d	112d		(2S,4S)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate	**1H NMR: (DMSO-d6) δ (ppm):** 10.45 (d, J=5.6 Hz, 1H), 10.24-10.22 (m, 1H), 8.85-8.82 (m ,1H), 8.66 (s, 1H), 8.61 (d, J=7.4 Hz, 1H), 8.39 (d, J=8.0 Hz, 1H), 7.66-7.54 (m, 3H), 7.37 (s, 1H), 7.29 (s, 1H), 7.07 (d, J=6.5 Hz, 1H), 6.83-6.78 (m, 1H), 5.23-4.94 (m, 2H), 4.54 (dd, J=26, 9.6 Hz, 1H), 4.16 (s, 1H), 3.68-3.56 (m, 5H), 2.22-2.18 (m, 1H), **2.05-1.98 (m, 2H).** **LRMS** (ESI): (calc.) 478.2; (found) 479.3 (MH) +.

Scheme 21



Example 110

(R)-2-(4-((2-(3,4-Difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)phenyl)-N-hydroxyacetamide (Compound 114)

Step 1: (R)-Ethyl 2-(4-((2-(3,4-difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)phenyl)acetate (Compound **113**)

[0222] Following the same procedure described in Example **16**, step 3, Scheme 1, but substituting Compound **$52b_{16}$** for acid **3a**, and ethyl 2-(4-formylphenyl)acetate (prepared according to the method of L.G. Goossen, *Chem. Commun.* **2001**, *7*, 669-670) for 4-methoxybenzaldehyde, compound **113** was isolated in 91% yield. LRMS (ESI): (calc.) 450.2; (found) 451.2 $(MH)^+$.

Step 2: (R)-2-(4-((2-(3,4-Difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)phenyl)-N-hydroxyacetamide (Compound **114**)

[0223] To a solution of **113** (260 mg, 0.58 mmol) in 1:1 THF/methanol (2.8 mL) was added a 50 %wt solution of hydroxylamine in water (3 mL). Sodium hydroxide powder (185 mg, 4.6 mmol) was then added to the mixture. After stirring at room temperature for 15 min the reaction was concentrated under vacuum. The product was purified by flash chromatography eluting with 10% MeOH/CH_2Cl_2. Compound **114** was isolated as beige solid (42 mg, 17%). ^{1}H NMR: (DMSO-d_6) δ (ppm): 10.62 (s, 1H), 10.46 (s, 1H), 8.79 (s, 1H), 7.24-7.08 (m, 6H), 6.87-6.84 (m, 1H), 6.76 (t, J = 6.3 Hz, 1H), 6.69 (d, J = 6.5 Hz, 1H), 6.60 (t, J = 6.8 Hz, 2H), 4.51 (d, J = 15.3 Hz, 1H), 4.20 (d, J = 15.5 Hz, 1H), 4.07 (t, J = 6.5 Hz, 1H), 3.21 (s, 2H), 2.81 (dd, J = 13.7, 6.5 Hz, 1H), 2.73 (dd, J = 13.7, 6.6 Hz, 1H). LRMS (ESI): (calc.) 437.2; (found) 438.2 $(MH)^+$.

Example 111

(R)-2-(3,4-Difluorobenzyl)-N-(4-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide (Compound 116)

Step 1: (R)-Ethyl 4-(2-(3,4-difluorobenzyl)-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-carboxamido)benzoate (Compound **115**)

[0224] To a solution of **52b$_{16}$** (137 mg, 0.50 mmol) in toluene (5 mL) was added ethyl 4-isocyanatobenzoate (478 mg, 2.5 mmol). The reaction was stirred at 80°C for 16 h, then THF (5 mL) was added and the reaction was stir at 70°C for 30 min. Polymer supported-trisamine (1.11 g, 4.0 mmol) was added and the mixture was stirred for 30 min at room temperature, then it was filtrated, and concentrated. The product was then purified by flash chromatography eluting with 60% AcOEt/hexane. Compound **115** was isolated (165 mg, 71%). LRMS (ESI): (calc.) 465.1; (found) 466.1 $(MH)^+$.

Step 2: (R)-2-(3,4-Difluorobenzyl)-N-(4-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide (Compound **116**)

[0225] Following the same procedure described in Example **110,** step 2, Scheme 21, but substituting compound **115** for compound **113**, compound **116** was isolated as a white solid in 34% yield. ^{1}H NMR: (DMSO-d_6) δ (ppm): 11.04 (bs, 1H), 10.83 (s, 1H), 9.07 (s, 1H), 8.91 (bs, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8. 8Hz, 2H), 7.37-7.32 (m, 1H), 7.26 (dt, J = 11, 8.4 Hz, 1H), 7.19-7.13 (m, 1H), 7.13 (t, J = 6.1 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 6.90-6.87 (m, 1H), 4.99 (dd, J = 8.8, 5.7 Hz, 1H), 2.87 (dd, J = 13.7, 5.5 Hz, 1H), 2.64 (dd, J = 13.8, 9.0 Hz, 1H). LRMS (ESI): (calc.) 452.1; (found) 453.1 $(MH)^+$.

Example 112

(R)-2-(3,4-difluorobenzyl)-N-(3-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide **(Compound 118)**

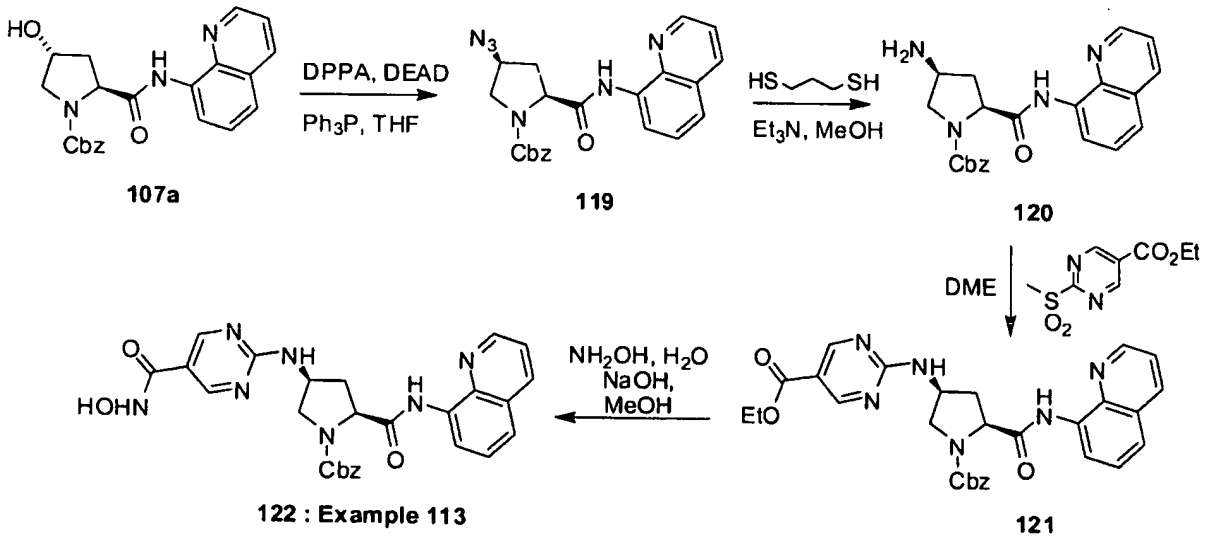
Step 1: (R)-Ethyl 3-(2-(3,4-difluorobenzyl)-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-carboxamido)benzoate (compound **117**)

[0226] Following the same procedure described in Example **111**, step 1, Scheme 21, but substituting ethyl 3-isocyanatobenzoate for ethyl 4-isocyanatobenzoate, compound **117** was isolated in 60% yield. LRMS (ESI): (calc.) 465.1; (found) 466.1 $(MH)^+$.

Step 2: (R)-2-(3,4-difluorobenzyl)-N-(3-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide (Compound **118**)

[0227] Following the same procedure described in Example **110**, step 2, Scheme 21, but substituting compound **117** for compound **114**, compound **118** was isolated in 7% yield. ^1H NMR: (DMSO-d_6) δ (ppm): 11.13 (bs, 1H), 10.81 (s, 1H), 9.00 (s, 2H), 7.73 (s, 1H), 7.47 (d, J = 7.2 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.31-7.22 (m, 3H), 7.19-7.16 (m, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 6.92-6.88 (m, 1H), 5.00 (dd, J = 8.6, 5.7 Hz, 1H), 2.86 (dd, J = 13.7, 5.9 Hz, 1H), 2.65 (dd, J = 13.7, 8.6 Hz, 1H). LRMS (ESI): (calc.) 452.1; (found) 453.1 $(MH)^+$.

Scheme 22



Example 113

(2S,4S)-Benzyl 4-(5-(hydroxycarbamoyl)pyrimidin-2-ylamino)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound 122)

Step 1: (2S,4S)-Benzyl 4-azido-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **119**)

[0228] To a solution of compound **107a** (500 mg, 1.28 mmol) in THF (13 mL) was added triphenylphosphine (402 mg, 1.54 mmol). The solution was cooled to 0°C, and diethyl

azodicarboxylate (0.26 mL, 1.66 mmol) was added, followed by diphenylphosphoryl azide (0.33 mL, 1.54 mmol). The reaction was allowed to warm slowly to room temperature over 1 h, and it was stirred for an additional 16 h. The solution was evaporated and the crude residue was purified by flash column chromatography on silica gel, eluting with a gradient of 20-40% AcOEt/hexane to afford compound **119** (409 mg, 77%): LRMS (ESI): (calc.) 416.2; (found) 417.2 $(MH)^+$.

Step 2: (2S,4S)-Benzyl 4-amino-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **120**)

[0229] Triethylamine (0.69 mL, 4.92 mmol) and 1,3-propanedithiol (0.49 mL, 4.92 mmol) were added to a stirred solution of Compound **119** (409 mg, 0.98 mmol) in MeOH (6.8 mL) at 0°C. The mixture was stirred for 16 h at room temperature. The solvent was evaporated, EtOAc and sat. aq. $NaHCO_3$ were added. The aqueous layer was extracted twice with EtOAc. The organic extracts were washed with brine, dried with $MgSO_4$, and filtered. The solution was evaporated and the crude residue was purified by flash column chromatography on silica gel, using a gradient of 0-10% $MeOH/CH_2Cl_2$ to afford compound **120** (250 mg, 65%): LRMS (ESI): (calc.) 390.2; (found) 391.2 $(MH)^+$.

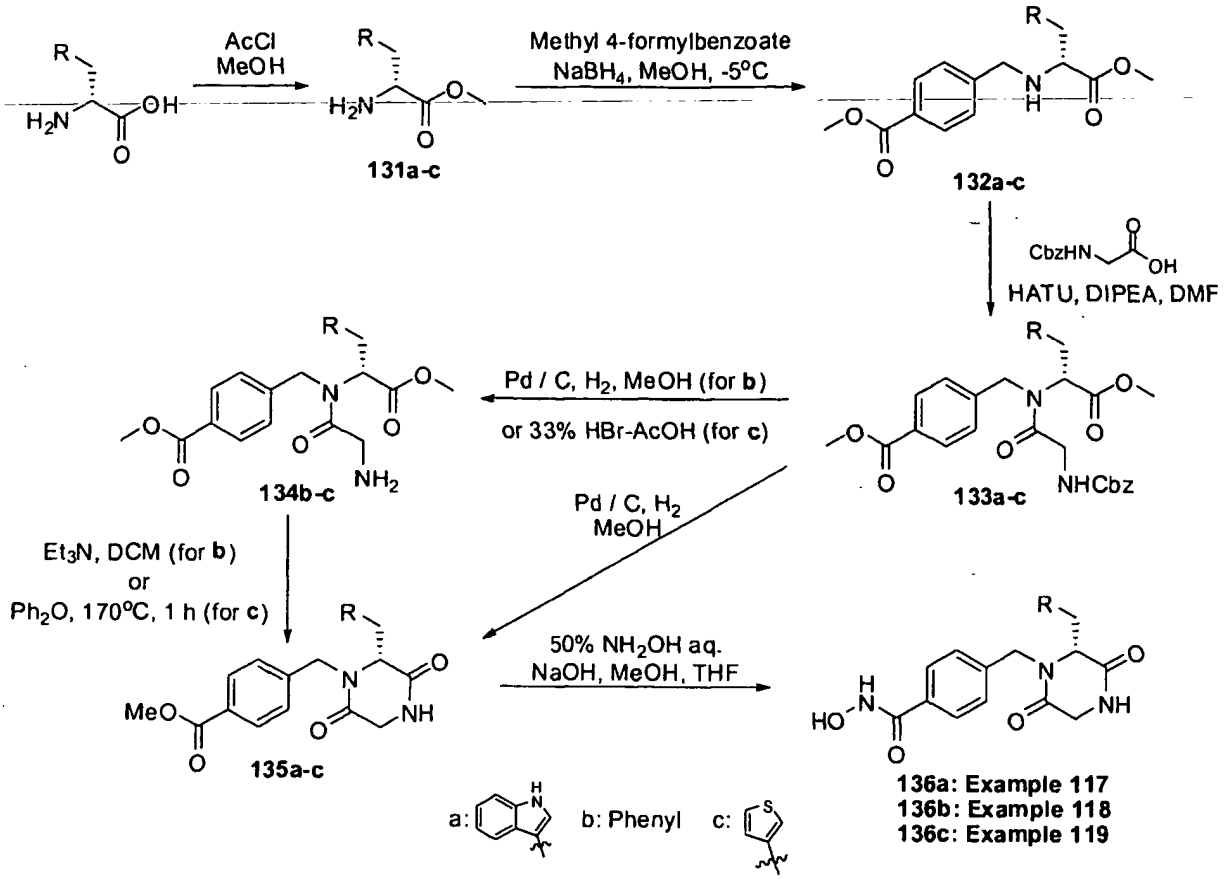
Step 3: (2S,4S)-Benzyl 4-(4-(methoxycarbonyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **121**)

[0230] Ethyl 2-(methylsulfonyl)pyrimidine-5-carboxylate (49 mg, 0.21 mmol) was added to a solution of compound **120** (83 mg, 0.21 mmol) in ethylene glycol dimethyl ether (1.0 mL). The mixture was stirred at 80°C for 16 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the aqueous layer was extracted with EtOAc three times. The organic extracts were dried with $MgSO_4$, filtered, and evaporated to give crude **121**. LRMS (ESI): (calc.) 540.2; (found) 541.3 $(MH)^+$.

Step 4: (2S,4S)-Benzyl 4-(5-(hydroxycarbamoyl)pyrimidin-2-ylamino)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Compound **122**)

[0231] Following the same procedure described in Example **108a**, step 4, Scheme 19, but substituting compound **121** for compound **108a**, compound was isolated as a beige solid in 15% yield. ^1H NMR: (DMSO-d_6) δ (ppm): 11.04 (bs, 1H), 10.46 (d, J = 14 Hz, 1H), 9.02 (bs, 1H), 8.88 (bs, 1H), 8.72-8.58 (m, 3H), 8.42 (dd, J = 8.2, 1.6 Hz, 1H), 7.98 (t, J = 7.0 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.67-7.58 (m, 2H), 7.42-7.28 (m, 2H), 7.11 (d, J = 7.4 Hz, 1H), 6.96 (t, J = 7.2 Hz, 1H), 6.81 (t, J = 7.4 Hz, 1H), 5.10 (s, 1H), 5.09-4.93 (m, 1H), 4.85-4.73 (m, 1H), 4.60-4.49 (m, 1H), 4.00 (t, J = 8.4 Hz, 1H), 3.38-3.33 (m, 1H), 2.77-2.66 (m, 1H), 2.15-2.08 (m, 1H). LRMS (ESI): (calc.) 527.2; (found) 528.3 $(MH)^+$.

Scheme 25



Example 117

(R)-4-((2-((1H-Indol-3-yl)methyl)-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxybenzamide (Compound 136a)

Step 1: (R)-Methyl 4-((3-(1H-indol-3-yl)-1-methoxy-1-oxopropan-2-ylamino)methyl)-benzoate (Compound **132a**)

[0232] (R)-Methyl 2-amino-3-(1H-indol-3-yl)propanoate hydrochloride (2.4 g, 9.4 mmol) was dissolved in DCM, washed with 10% $NH_4OH_{(aq)}$, dried over sodium sulfate and concentrated. The free amine **131a** obtained was dissolved in MeOH (10 mL) with methyl 4-formylbenzoate (1.2 g, 11.3 mmol) and stirred for 3 h at room temperature. $NaBH_4$ (1.1 g, 10.3 mmol) was then added at -5°C and the reaction mixture was stirred over night in a -20°C freezer. The reaction was quenched by adding ice and water, the MeOH was evaporated and the product was extracted with DCM (3x), dried over sodium sulfate and concentrated to afford the title compound **132a** (1.4 g, 41%). LRMS (ESI): (calc.) 366.2; (found) 367.3 $(MH)^+$.

Step 2: (R)-Methyl 4-((N-(3-(1H-indol-3-yl)-1-methoxy-1-oxopropan-2-yl)-2-(benzyl-oxycarbonylamino)acetamido)methyl)benzoate (Compound **133a**)

[0233] DIPEA (0.28 mL, 1.62 mmol) was added to a solution of HATU (0.62 g, 1.62 mmol) and 2-(benzyloxycarbonylamino)acetic acid (0.34 g, 1.62 mmol) in DMF (3 mL) at

0°C. The solution was stirred 10 min then the amine 132a (0.54 g, 1.47 mmol) was added and stirred over night at room temperature. The solution was diluted with AcOEt, washed with water, 1N HCl (x2), $NaHCO_{3(aq)}$ and brine, dried over sodium sulfate and concentrated to afford the title compound **133a** as a foam (0.8 g, 97%). LRMS (ESI): (calc.) 557.2; (found) 558.4 $(MH)^+$.

Step 3: (R)-Methyl 4-((2-((1H-indol-3-yl)methyl)-3,6-dioxopiperazin-1-yl)methyl)-benzoate (Compound **135a**)

[0234] Following the procedure described in Example 1, **4a**, step 2 (Scheme 1) but substituting Compound **133a** for **2a**, the title Compound **135a** was obtained as a beige solid (0.23 g, 39%). LRMS (ESI): (calc.) 391.2; (found) 392.2 $(MH)^+$.

Step 4: (R)-4-((2-((1H-Indol-3-yl)methyl)-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxy-benzamide (Compound **136a**)

[0235] Following the same procedure described in Example **108a,** step 4, Scheme 19, but substituting compound **135a** for compound **108a**, the title compound **136a** was isolated as white powder (1 mg, 0.1%). LRMS: (calc) 392.2 (found) 393.1 $(MH)^+$. ^1H NMR (MeOD-d_4) δ(ppm): 11.16 (s, 1H), 10.99 (s, 1H), 9.02 (s, 1H), 7.88 (d, J = 3.3 Hz, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.08-7.01 (m, 2H), 6.95 (t, J = 7.5 Hz, 1H), 5.15 (d, J = 15.1 Hz, 1H), 4.15-4.02 (m, 2H), 3.91 (t, J = 4.3 Hz, 1H), 3.3-3.2 (m, 2H).

Example 118

(R)-4-((2-Benzyl-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxybenzamide (Compound 136b)

Step 1: (R)-Methyl 4-((1-methoxy-1-oxo-3-phenylpropan-2-ylamino)methyl)benzoate (Compound **132b**)

[0236] Following the same procedure described in Example 117, step 1, Scheme 25, but substituting compound **131b** for compound **131a**, the title compound **132b** was isolated as an oil (0.85 g, 49%). ^1H NMR ($CDCl_3$) δ(ppm): 8.00-7.88 (m, 2H), 7.39-7.05 (m, 7H), 4.01-3.75 (m, 2H), 3.90 (s, 3H), 3.66 (s, 3H), 3.65-3.55 (m, 1H), 3.10-3.00 (m, 2H).

Step 2: (R)-Methyl 4-((2-(benzyloxycarbonylamino)-N-(1-methoxy-1-oxo-3-phenyl-propan-2-yl)acetamido)methyl)benzoate (Compound **133b**)

[0237] Following the same procedure described in Example 117, step 2, Scheme 25, but substituting compound **132b**, HATU and DIPEA for compound **132a**, EDCI and HOBt, the title compound **133b** was isolated as an oil (0.7 g, 54%). LRMS (ESI): (calc.) 518.2; (found) 519.6 $(MH)^+$.

Step 3: (R)-Methyl 4-((2-amino-N-(1-methoxy-1-oxo-3-phenylpropan-2-yl)-acetamido)methyl)benzoate (Compound **134b**)

[0238] Following the same procedure described in Example 117, step 3, Scheme 25, but substituting compound **133b** for compound **133a**, the title compound **134b** was obtained and used without purification. LRMS (ESI): (calc.) 384.2; (found) 385.1 $(MH)^+$.

Step 4: (R)-Methyl 4-((2-benzyl-3,6-dioxopiperazin-1-yl)methyl)benzoate (Compound **135b**)

[0239] A solution of compound **134b** (1.35 mmol) and Et_3N (1 mL, 7.3 mmol) in DCM (10 mL) was stirred at room temperature over night. The solution was diluted in DCM, washed with saturated $NaHCO_{3(aq)}$, dried over sodium sulfate and concentrated to afford the title compound **135b** (120 mg, 25%, yield for two steps). LRMS (ESI): (calc.) 352.1; (found) 353.2 $(MH)^+$.

Step 5: (R)-4-((2-Benzyl-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxybenzamide (Compound **136b**)

[0240] Following the same procedure described in Example **108a**, step 4, Scheme 19, but substituting compound **135b** for compound **108a**, the title compound **136b** was isolated as white powder (6 mg, 12%). LRMS: (calc) 353.1 (found) 353.1 $(MH)^+$. ^1H NMR (DMSO-d_6) δ(ppm): 11.16 (s, 1H), 9.01 (s, 1H), 8.07 (d, J = 6.5 Hz, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.30-7.28 (m, 3H), 7.12-7.10 (m, 1H), 5.13 (d, J = 15 Hz, 1H), 4.07 (d, J = 15 Hz, 1H), 3.95 (t, J = 4.6 Hz, 1H), 3.4-3.3 (m, 2H), 3.23 (dd, J = 12.9, 5.5 Hz, 1H), 3.04 (dd, J = 4.1, 3.7 Hz, 1H).

Example 119

(R)-4-((3,6-Dioxo-2-(thien-2-ylmethyl)piperazin-1-yl)methyl)-N-hydroxybenzamide (Compound 136c)

Step 1: (R)-Methyl 2-amino-3-(thien-2-yl)propanoate (Compound **131c**)

[0241] AcCl (4.15 mL, 58.5 mmol) was added dropwise in MeOH (50 mL) at 0°C. The solution was stirred 15 min then (R)-2-amino-3-(thiophen-2-yl)propanoic acid (2.0 g, 11.7 mmol) was added and stirred over night. The solvent was concentrated and the residue was dissolved in DCM, washed with $NaHCO_{3(aq)}$, dryed with sodium sulfate and concentrated under vacuum to afford the title compound **131c** (1.5 g, 69%). LRMS (ESI): (calc.) 185.4; (found) 186.1 $(MH)^+$.

Step 2: (R)-Methyl 4-((1-methoxy-1-oxo-3-(thien-2-yl)propan-2-ylamino)methyl)-benzoate (Compound **132c**)

[0242] Following the same procedure described in Example 117, step 1, Scheme 25, but substituting compound **131c** for compound (R)-Methyl 2-amino-3-(1H-indol-3-yl)propanoate, the title compound **132c** was isolated (0.81 g, 45%). LRMS (ESI): (calc.) 333.1; (found) 334.1 $(MH)^+$.

Step 3: (R)-Methyl 4-((2-(benzyloxycarbonylamino)-N-(1-methoxy-1-oxo-3-(thien-2-yl)propan-2-yl)acetamido)methyl)benzoate (Compound **133c**)

[0243] Following the same procedure described in Example 117, step 2, Scheme 25, but substituting compound **132c** for compound **132a**, the title compound **133c** was isolated as (0.64 g, 81%). LRMS (ESI): (calc.) 524.6; (found) 525.7 $(MH)^+$.

Step 4: (R)-Methyl 4-((2-amino-N-(1-methoxy-1-oxo-3-(thien-2-yl)propan-2-yl)acetamido)methyl)benzoate hydrobromide (Compound **134c**)

[0244] A solution of compound 133c (0.68 g, 2.7 mmol) and 33% HBr in AcOH (5 mL) was prepared at 0°C and stirred 1 h at room temerature. The solution was concentrated and triturated in Et_2O (3x) to afford title compound **134c** (0.8 g, 63%). LRMS (ESI): (calc.) 390.1; (found) 391.3 $(MH)^+$.

Step 5: (R)-Methyl 4-((3,6-dioxo-2-(thien-2-ylmethyl)piperazin-1-yl)methyl)-benzoate (Compound **135c**)

[0245] Compound **134c** (0.8 g, 1.7 mmol) was dissolved in DCM, washed with 10% $NH_4OH_{(aq)}$, dried over sodium sulfate and concentrated. The free amine obtained was dissolved in phenyl ether (5 mL) and stirred at 170°C for 1 h. The solution was cooled down, diluted with hexanes and stirred 20 min. The precipitate obtain was filtered, rinsed with hexanes to afford the title compound as a beige solid (0.8 g, 100%). LRMS: (calc) 358.1 (found) 359.5 $(MH)^+$.

Step 6: (R)-4-((3,6-Dioxo-2-(thien-2-ylmethyl)piperazin-1-yl)methyl)-N-hydroxy-benzamide (Compound **136c**)

[0246] Following the same procedure described in Example **108a**, step 4, Scheme 19, but substituting compound **135c** for compound **108a**, the title compound **136c** was isolated as a beige solid (130 mg, 100%). LRMS: (calc) 359.1 (found) 360.1 $(MH)^+$. ^1H NMR (DMSO-d_6) δ(ppm): 11.16 (s, 1H), 9.01 (s, 1H), 8.14 (s, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.46 (d, J = 5.1 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 6.98 (t, J = 3.7 Hz, 1H), 6.79 (s, 1H), 5.11 (d, J = 15.4 Hz, 1H), 4.14 (d, J = 14.8 Hz, 1H), 4.03 (s, 1H), 3.95 (s, 1H), 3.46 (d, J = 15.1 Hz, 1H), 3.3-3.2 (m, 1H), 2.72 (d, J = 17.4 Hz, 1H).

Compositions

[0247] In the third aspect, the invention provides compositions comprising an inhibitor of histone deacetylase according to the invention and a pharmaceutically acceptable carrier, excipient, or diluent. Compounds of the invention may be formulated by any method known in the art and may be prepared for administration by any route, including, without limitation, parenteral, oral, sublingual, transdermal, topical, intranasal, intratracheal, or intrarectal. In certain preferred embodiments, compounds of the invention are administered intravenously in a hospital setting. In certain other preferred embodiments, administration may preferably

be by the oral route. The compositions may be in any form, including but not limited to liquid solutions or suspensions; for oral administration, formulations may be in the form of tablets or capsules; and for intranasal formulations, in the form of powders, nasal drops or aerosols. The compositions may be administered locally or systemically.

[0248] The characteristics of the carrier will depend on the route of administration. As used herein, the term "pharmaceutically acceptable" means a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism, and that does not interfere with the effectiveness of the biological activity of the active ingredient(s). Thus, compositions according to the invention may contain, in addition to the inhibitor, diluents, fillers, salts, buffers, stabilizers, solubilizers, or other materials well known in the art. The preparation of pharmaceutically acceptable formulations is described in, e.g., Remington's Pharmaceutical Sciences, 18th Edition, ed. A. Gennaro, Mack Publishing Co., Easton, PA, 1990.

[0249] As used herein, the term pharmaceutically acceptable salts refer to salts that retain the desired biological activity of the above-identified compounds and exhibit minimal or no undesired toxicological effects. Examples of such salts include, but are not limited to acid addition salts formed with inorganic acids (for example, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, and the like), and salts formed with organic acids such as acetic acid, oxalic acid, tartaric acid, succinic acid, malic acid, ascorbic acid, benzoic acid, tannic acid, pamoic acid, alginic acid, polyglutamic acid, naphthalenesulfonic acid, naphthalenedisulfonic acid, and polygalacturonic acid. The compounds can also be administered as pharmaceutically acceptable quaternary salts known by those skilled in the art, which specifically include the quaternary ammonium salt of the formula -NR + Z-, wherein R is hydrogen, alkyl, or benzyl, and Z is a counterion, including chloride, bromide, iodide, -O-alkyl, toluenesulfonate, methylsulfonate, sulfonate, phosphate, or carboxylate (such as benzoate, succinate, acetate, glycolate, maleate, malate, citrate, tartrate, ascorbate, benzoate, cinnamoate, mandeloate, benzyloate, and diphenylacetate). As used herein, the term "salt" is also meant to encompass complexes, such as with an alkaline metal or an alkaline earth metal.

[0250] The active compound is included in the pharmaceutically acceptable carrier or diluent in an amount sufficient to deliver an HDAC inhibiting effective amount without causing serious toxic effects. The effective dosage range of the pharmaceutically acceptable derivatives can be calculated based on the weight of the parent compound to be delivered. If the derivative exhibits activity in itself, the effective dosage can be estimated as above using the weight of the derivative, or by other means known to those skilled in the art.

[0251] In certain preferred embodiments of the second aspect of the invention, the composition further comprises an antisense oligonucleotide that inhibits the expression of a histone deacetylase gene. The combined use of a nucleic acid level inhibitor (e.g., antisense oligonucleotide) and a protein level inhibitor (i.e., inhibitor of histone deacetylase enzyme activity) results in an improved inhibitory effect, thereby reducing the amounts of the inhibitors required to obtain a given inhibitory effect as compared to the amounts necessary when either is used individually. The antisense oligonucleotide according to this aspect of the invention is complementary to regions of RNA or double-stranded DNA that encode one or more of HDAC-1, HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7, HDAC-8, HDAC-9, HDAC-10, HDAC-11, SirT1, SirT2, SirT3, SirT4, SirT5, SirT6 and SirT7 (see e.g., GenBank Accession Number U50079 for HDAC-1, GenBank Accession Number U31814 for HDAC-2, and GenBank Accession Number U75697 for HDAC-3).

Inhibition of Histone Deacetylase

[0252] In the fourth aspect, the present invention provides a method of inhibiting histone deacetylase, comprising contacting the histone deacetylase with an inhibition effective amount of an inhibitor of histone deacetylase of the present invention.

[0253] In a preferred embodiment of the fourth aspect of the invention, the invention provides a method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase according to the invention or a composition comprising an inhibitor of histone decetylase according to the invention. Because compounds of the invention inhibit histone deacetylase, they are useful research tools for the study of histone deacetylases and their role in biological processes.

[0254] Measurement of the enzymatic activity of a histone deacetylase can be achieved using known methodologies. For example, Yoshida et al., J. Biol. Chem., **265**: 17174-17179 (1990), describes the assessment of histone deacetylase enzymatic activity by the detection of acetylated histones in trichostatin A treated cells. Taunton et al., Science, **272**: 408-411 (1996), similarly describes methods to measure histone deacetylase enzymatic activity using endogenous and recombinant HDAC-1.

[0255] In some preferred embodiments, the histone deacetylase inhibitor interacts with and reduces the activity of all histone deacetylases in a cell. In some other preferred embodiments according to this aspect of the invention, the histone deacetylase inhibitor interacts with and reduces the activity of fewer than all histone deacetylases in the cell. In certain preferred embodiments, the inhibitor interacts with and reduces the activity of one histone deacetylase (e.g., HDAC-1), but does not interact with or reduce the activities of

other histone deacetylases (e.g., HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7, HDAC-8, HDAC-9, HDAC-10, HDAC-11, SirT1, SirT2, SirT3, SirT4, SirT5, SirT6 and SirT7).

[0256] For purposes of the invention, the term "oligonucleotide" includes polymers of two or more deoxyribonucleosides, ribonucleosides, or 2'-substituted ribonucleoside residues, or any combination thereof. Preferably, such oligonucleotides have from about 6 to about 100 nucleoside residues, more preferably from about 8 to about 50 nucleoside residues, and most preferably from about 12 to about 30 nucleoside residues. The nucleoside residues may be coupled to each other by any of the numerous known internucleoside linkages. Such internucleoside linkages include without limitation phosphorothioate, phosphorodithioate, alkylphosphonate, alkylphosphonothioate, phosphotriester, phosphoramidate, siloxane, carbonate, carboxymethylester, acetamidate, carbamate, thioether, bridged phosphoramidate, bridged methylene phosphonate, bridged phosphorothioate and sulfone internucleoside linkages. In certain preferred embodiments, these internucleoside linkages may be phosphodiester, phosphotriester, phosphorothioate, or phosphoramidate linkages, or combinations thereof. The term oligonucleotide also encompasses such polymers having chemically modified bases or sugars and/ or having additional substituents, including without limitation lipophilic groups, intercalating agents, diamines and adamantane.

[0257] For purposes of the invention the term "2'-substituted ribonucleoside" includes ribonucleosides in which the hydroxyl group at the 2' position of the pentose moiety is substituted to produce a 2'-O-substituted ribonucleoside. Preferably, such substitution is with a lower alkyl group containing 1-6 saturated or unsaturated carbon atoms, or with an aryl or allyl group having 2-6 carbon atoms, wherein such alkyl, aryl or allyl group may be unsubstituted or may be substituted, e.g., with halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, or amino groups. The term "2'-substituted ribonucleoside" also includes ribonucleosides in which the 2'-hydroxyl group is replaced with an amino group or with a halo group, preferably fluoro.

[0258] Particularly preferred antisense oligonucleotides utilized in this aspect of the invention include chimeric oligonucleotides and hybrid oligonucleotides.

[0259] For purposes of the invention, a "chimeric oligonucleotide" refers to an oligonucleotide having more than one type of internucleoside linkage. One preferred example of such a chimeric oligonucleotide is a chimeric oligonucleotide comprising a phosphorothioate, phosphodiester or phosphorodithioate region, preferably comprising from about 2 to about 12 nucleotides, and an alkylphosphonate or alkylphosphonothioate region (see e.g., Pederson et al. U.S. Patent Nos. 5,635,377 and 5,366,878). Preferably, such chimeric oligonucleotides contain at least three consecutive internucleoside linkages selected from phosphodiester and phosphorothioate linkages, or combinations thereof.

[0260] For purposes of the invention, a "hybrid oligonucleotide" refers to an oligonucleotide having more than one type of nucleoside. One preferred example of such a hybrid oligonucleotide comprises a ribonucleotide or 2'-substituted ribonucleotide region, preferably comprising from about 2 to about 12 2'-substituted nucleotides, and a deoxyribonucleotide region. Preferably, such a hybrid oligonucleotide contains at least three consecutive deoxyribonucleosides and also contains ribonucleosides, 2'-substituted ribonucleosides, preferably 2'-O-substituted ribonucleosides, or combinations thereof (see e.g., Metelev and Agrawal, U.S. Patent No. 5,652,355).

[0261] The exact nucleotide sequence and chemical structure of an antisense oligonucleotide utilized in the invention can be varied, so long as the oligonucleotide retains its ability to inhibit expression of the gene of interest. This is readily determined by testing whether the particular antisense oligonucleotide is active. Useful assays for this purpose include quantitating the mRNA encoding a product of the gene, a Western blotting analysis assay for the product of the gene, an activity assay for an enzymatically active gene product, or a soft agar growth assay, or a reporter gene construct assay, or an *in vivo* tumor growth assay, all of which are known in the art, or are as described in detail in this specification or in, for example, Ramchandani et al. (1997) Proc. Natl. Acad. Sci. USA 94: 684-689.

[0262] Antisense oligonucleotides utilized in the invention may conveniently be synthesized on a suitable solid support using well known chemical approaches, including H-phosphonate chemistry, phosphoramidite chemistry, or a combination of H-phosphonate chemistry and phosphoramidite chemistry (i.e., H-phosphonate chemistry for some cycles and phosphoramidite chemistry for other cycles). Suitable solid supports include any of the standard solid supports used for solid phase oligonucleotide synthesis, such as controlled-pore glass (CPG) (see, e.g., Pon, R.T. (1993) Methods in Molec. Biol. 20: 465-496).

[0263] Particularly preferred oligonucleotides have nucleotide sequences of from about 13 to about 35 nucleotides which include the nucleotide sequences shown in Table 13. Yet additional particularly preferred oligonucleotides have nucleotide sequences of from about 15 to about 26 nucleotides and comprise the nucleotide sequences shown in Table 13.

Table 13

Oligo	Target	Accession Number	Nucleotide Position	Sequence	position within Gene	Seq ID No.
HDAC1 AS1 HDAC1 AS2	Human HDAC1 Human HDAC1	U50079 U50079	1585-1604 1565-1584	5'-GAAACGTGAGGGACTCAGCA-3' 5'-GGAAGCCAGAGCTGGAGAGG-3'	3'-UTR 3'-UTR	Seq ID No:1 Seq ID No:2
HDAC2 AS	Human HDAC2	U31814	1643-1622	5'-GCTGAGCTGTTCTGATTTGG-3'	3'-UTR	Seq ID No:3
HDAC3 AS	Human HDAC3	AF039703	1276-1295	5'-CGCTTTCCTTGTCATTGACA-3'	3'-UTR	Seq ID No:4
HDAC4 AS1 HDAC4 AS2	Human HDAC4 Human HDAC4	AB006626 AB006626	514-33 7710-29	5-GCTGCCTGCCGTGCCCACCC-3' 5'-TACAGTCCATGCAACCTCCA-3'	5'-UTR 3'-UTR	Seq ID No:5 Seq ID No:6
HDAC5 AS	Human HDAC5	AF039691	2663-2682	5'-CTTCGGTCTCACCTGCTTGG-3'	3'-UTR	Seq ID No:7
HDAC6 AS	Human HDAC6	AJ011972	3791-3810	5'-CAGGCTGGAATGAGCTACAG-3'	3'-UTR	Seq ID No:8
HDAC7 AS	Human HDAC7	AF239243	2896-2915	5'-CTTCAGCCAGGATGCCCACA-3'	3'-UTR	Seq ID No:9
HDAC8 AS1 HDAC8 AS2	Human HDAC8 Human HDAC8	AF230097 AF230097	51-70 1328-1347	5'-CTCCGGCTCCTCCATCTTCC-3' 5'-AGCCAGCTGCCACTTGATGC-3'	5'-UTR 3'-UTR	Seq ID No:10 Seq ID No:11

[0264] In certain preferred embodiments of the invention, the antisense oligonucleotide and the HDAC inhbitor of the present invention are administered separately to a mammal, preferably a human. For example, the antisense oligonucleotide may be administered to the mammal prior to administration to the mammal of the HDAC inhibitor of the present invention. The mammal may receive one or more dosages of antisense oligonucleotide prior to receiving one or more dosages of the HDAC inhibitor of the present invention.

[0265] In another example, the HDAC inhibitor of the present invention may be administered to the mammal prior to administration of the antisense oligonucleotide. The mammal may receive one or more dosages of the HDAC inhibitor of the present invention prior to receiving one or more dosages of antisense oligonucleotide.

[0266] In certain preferred embodiments of the present invention, the HDAC inhibitor of the present invention may be administered together with other HDAC inhibitors known in the art or which will be discovered. Administration of such HDAC inhibitors may be done sequentially or concurrently. In certain preferred embodiments of the present invention the compositions comprise HDAC inhibitors of the present invention and/or an antisense oligonucleotide and/or another HDAC inhibitor known in the art or which will be discovered. The active ingredients of such compositions may act synergistically to inhibit histone deacetylase.

[0267] In certain embodiments, the known HDAC inhibitor is selected from the group consisting of, but not limited to, trichostatin A, depudecin, trapoxin, suberoylanilide hydroxamic acid, FR901228, MS-27-275, CI-994 sodim butyrate, MGCD0103, and those compounds found in WO 2003/024448, WO 2004/069823, WO 2001/038322, US 6,541,661, WO 01/70675, WO 2004/035525 and WO 2005/030705.

[0268] The following Examples are intended to further illustrate certain preferred embodiments of the invention, and are not intended to limit the scope of the invention.

ASSAY EXAMPLES

Assay Example 1

Inhibition of Histone Deacetylase Enzymatic Activity

[0269] The following protocol is used to assay the compounds of the invention. In the assay, the buffer used is 25 mM HEPES, pH 8.0, 137 mM NaCl, 2.7 mM KCl, 1 mM $MgCl_2$ and the subtrate is Boc-Lys(Ac)-AMC in a 50 mM stock solution in DMSO. The enzyme stock solution is 4.08 µg/mL in buffer.

[0270] The compounds are pre-incubated (2µl in DMSO diluted to 13 µl in buffer for transfer to assay plate) with enzyme (20µl of 4.08µg/mL) for 10 min at room temperature (35µl pre-incubation volume). The mixture is pre-incubated for 5 min at room temperature. The reaction is started by bringing the temperature to 37°C and adding 16 µl substrate. Total

reaction volume is 50 µl. The reaction is stopped after 20 min by addition of 50µl developer, prepared as directed by Biomol (Fluor-de-Lys developer, Cat. # KI-105). A plate is incubated in the dark for 10 min at room temperature before reading (λ_{Ex}=360nm, λ_{Em}=470nm, Cutoff filter at 435nm).

[0271] Table 14 shows that HDAC inhibitors of the present invention have HDAC inhibitor activity (IC_{50}) against one or more of HDAC-1, HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7, HDAC-8, HDAC-9, HDAC-10, HDAC-11, SirT1, SirT2, SirT3, SirT4, SirT5, SirT6 and SirT7. In the table, "A" indicates inhibitory activity at a concentration of ≤ 0.05 μM; "B" indicates inhibitory activity at a concentration > 0.05 μM but ≤0.5 μM, "C" indicates inhibitory activity at > 0.5 μM but ≤2 μM and "D" indicates inhibitory activity at a concentration of > 2 μM but ≤10 μM.

Table 14

Cpd	HDAC Inhibitory Activity (IC_{50})
4k	D
66f	B
4h	D
6h	D
5c	D
23a	D
47b	D
47a	B
4c	C
24a	B
4b	D
62	B
49	B
97a	D
54b19	B
54b20	A
54c	B
68b7	D
24e	A
29a	B
68b9	C
68b6	C
68b1	C
68b11	B
79	B
74	B
68b12	B
4f	D
4a	D
4d	D

Cpd	HDAC Inhibitory Activity (IC_{50})
80	B
81	C
13	B
24f	A
8	C
4i	D
66c	C
92a	B
83	C
88a	B
26e	B
82	C
68b8	B
4g	D
69	C
43	D
16f	B
18a	D
18b	C
16a	D
16c	C
54a1	B
54a2	A
109b	B
112c	C
112b	C
68b22	C
54b10	A
16g	D
16d	D

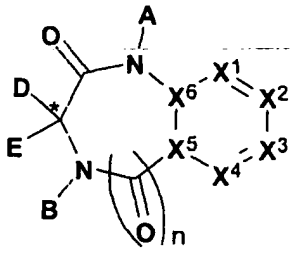
Cpd	HDAC Inhibitory Activity (IC_{50})
97k	D
4e	D
68b16	D
68b18	B
68b3	B
68b19	C
68b20	C
68b21	B
18c	D
18e	C
18f	C
109a	B
112a	C
16h	C
16b	C
16e	D
4l	C
109c	B
68b4	B
71	D
54b1	A
54b5	A
54b3	A
54b4	A
54b2	A
54b8	B
56a	C
54b9	A
54b11	A
54b12	A

Cpd	HDAC Inhibitory Activity (IC_{50})
54b13	A
54b14	B
68b23	B
54b7	A
54b15	A
54b16	A
54b17	B
97c	C
97h	C
54b21	A
72	D
54b18	A
92b	B
97b	D
97d	C
97f	D
97g	D
97i	D
97j	D
112d	B
136b	A
136a	A
136c	B
110	C
116	A
118	B
122	A

[0272] While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice within the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth, and as follows in the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A compound of the formula (I):



(I)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof,wherein

n is 0 or 1;

X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, C-Z and N, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z;

X^5-X^6 is C=C;

or

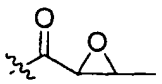
X^1, X^2, X^3 and X^4 are absent, X^5 is a covalent bond and X^6 is independently selected from the group consisting of CH_2 and CH(Z), with the provisio that an N, O or $S(O)_{0-1}$ in Z is separated from the CH of X^6 by at least two carbon atoms;

Z is independently selected from the group consisting of halo, $-CF_3$, $-NO_2$, -CN, $-(C_0-C_6)$alkyl-OR^1, $-(C_0-C_6)$alkyl-$N(R^1)_2$, $-(C_1-C_6)$alkyl, $-N(R^1)-C(O)-(C_1-C_6)$alkyl, $-N(R^1)-S(O)_2-(C_1-C_6)$alkyl, $-O-(C_2-C_6)$alkyl-$N(R^1)(R^1)$, $-S-R^1$, $-(C_0-C_6)$alkyl-$C(O)-OR^1$, $-N(R^1)-C(O)-CF_3$, $-N(R^1)-(C_2-C_6)$alkyl-$N(R^1)(R^1)$, $-(C_0-C_7)$alkyl-W, $-(C_2-C_7)$alkenyl-W, $-(C_2-C_7)$alkynyl-W, $-(C_0-C_5)$alkyl-CH=CH-W, $-C(O)-(C_1-C_7)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(S)-(C_1-C_6)$alkyl-W, $-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-O-(C_1-C_6)$alkyl-W, $-S(O)_2-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-S(O)_2-(C_1-C_6)$alkyl-W, $-C(O)-N(R^1)_2$, $-(C_0-C_3)$alkyl-$O-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$O-(C_1-C_6)$alkyl-W, $-(C_0-C_3)$alkyl-$S-(C_1-C_6)$alkyl-W, $-N(R^1)-C(O)-OR^1$, $-S(O)_2-N(R^1)_2$, $-N(R^1)-S(O)_2R^1$, $-(C_0-C_7)$alkyl-aryl-W, $-(C_0-C_7)$alkyl-heteroaryl-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-aryl, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-heteroaryl, -aryl, $-(C_1-C_6)$alkylaryl-, -heteroaryl, $-(C_1-C_6)$alkylheteroaryl-, $-(C_1-C_8)$heteroalkyl, $-(C_3-C_6)$cycloalkyl, $-(C_3-C_6)$heterocycloalkyl, $-(C_0-C_3)$alkyl-$N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)C(O)-O-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$O-C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$S(O)_2N(R^1)-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$N(R^1)S(O)_2-(C_0-C_3)$alkyl-aryl-$(CH=CH)_{0-1}$-W, $-(C_0-C_3)$alkyl-$C(O)N(R^1)-(C_0-C_3)$alkyl-aryl-

$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)N(R^1)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-(CH=CH)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-O-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-S-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-O-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-OC(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-S(O)$_2$N(R_1)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)S(O)$_2$-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W and -(C_0-C_3)alkyl-(CH=CH)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_5)alkyl-C≡C-W, -(C_0-C_3)alkyl-O-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-S-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-O-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-O-C(O)N(R^1)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-S(O)$_2$N(R^1)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)S(O)$_2$-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-C(O)N(R^1)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)N(R^1)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-aryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-(CH=CH)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-aryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-O-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-S-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-O-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-OC(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-S(O)$_2$N(R_1)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)S(O)$_2$-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-N(R^1)C(O)N(R^1)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-heteroaryl-$(CH=CH)_{0-1}$-W, -(C_0-C_3)alkyl-(CH=CH)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, -(C_0-C_3)alkyl-(C≡C)-(C_0-C_3)alkyl-heteroaryl-$(C≡C)_{0-1}$-W, (C_0-C_3)alkyl-C(O)-N(R^1)-(C_1-C_6)alkyl-W, (C_0-C_3)alkyl-C(S)-N(R^1)-(C_1-C_6)alkyl-W, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-aryl, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-heteroaryl, -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-N(R_1)-aryl, and -(C_0-C_3)alkyl-N(R_1)-C(O)-(C_1-C_6)alkyl-C(O)-N(R_1)-heteroaryl, wherein each of the aryl, heteroaryl, cycloalkyl and heterocyclyl moieties of the above-mentioned Z is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, -SH, mono- to per-halogenated -(C_1-C_6)alkyl, and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group;

R^1 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein each aryl, heteroaryl, cycloalkyl and heterocyclyl moiety of said -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, aryl, heteroaryl, mono- to per-halogenated-(C_1-C_6)alkyl and -(C_2-C_4)alkyl-N(R^1)$_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group;

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-C_1-C_4 alkyl, -C(O)-N(R^1)$_2$, -(C_1-C_6)alkyl-N(OH)-C(O)H-, -(C_1-C_6)alkyl-SR^1, -(C_1-C_6)alkyl-S-C(O)-(C_1-C_4)alkyl, -C(O)-OR^1,



-C(O)-(C_1-C_4)alkyl-SH, -C(O)-(C_1-C_4)alkyl-S-C(O)R^1, -C(O)-(C_1-C_4)alkyl-S-heteroaryl, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6) alkyl-halo, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SH, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SC(O)R^1, -C(O)-NH-(C_2-C_6)alkyl-SH, -C(O)-N(R^1)-(C_0-C_6)alkyl-SR^1, -C(O)-cycloalkyl, -C(O)-heterocyclyl, -C(O)-N(R^1)-aryl-Q, -C(O)-N(R^1)-heteroaryl-Q, -C(O)-aryl, -C(O)-heteroaryl and -C(O)-(C_1-C_6) alkyl wherein the alkyl is optionally substituted with one or more substituents selected from the group consisting of halo, mono to per-halogenated-(C_1-C_6)alkyl, -C(O)-heteroaryl, -C(O)-NH-heteroaryl and -C(O)-NH-aryl, wherein each aryl and heteroaryl moiety of the afore-mentioned W group is optionally substituted with one or more substituents selected from the group consisting of -NH_2, -OH, -SH, -CN, -NO_2, -N(R^1)$_2$, halo, mono- to per-halogenated -(C_1-C_6)alkyl, aryl and heteroaryl;

E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-(C_3-C_6)cycloalkyl, -(C_0-C_6)heteroalkyl-(C_3-C_6)cycloalkyl, -(C_0-C_6)alkyl-(C_3-C_6)heterocyclyl, -(C_0-C_6)heteroalkyl-(C_3-C_6)heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)alkyl-heteroaryl-(C_0-C_3)alkyl-aryl, -(C_0-C_6)alkyl-aryl-(C_0-C_3)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl-(C_0-C_3)alkyl-heteroaryl, -(C_0-C_6)alkyl-aryl-(C_0-C_3)alkyl-heteroaryl, heterocyclyl, -(C_1-C_6)alkyl-S-R^1, -(C_1-C_6)heteroalkyl-S-R^1, -(C_1-C_6)alkyl-O-R^1, -(C_1-C_6)heteroalkyl-O-R^1, -C_1-C_6 alkyl-W, -(C_1-C_6)heteroalkyl-W, -(C_1-C_6)alkyl-M-(C_1-C_3)alkyl-W, -(C_1-C_6)heteroalkyl-M-(C_1-C_3)alkyl-W, -(C_1-C_6)alkyl-N(R^1)$_2$, -(C_1-C_6)heteroalkyl-N(R^1)$_2$, -(C_1-C_6)alkyl-N(R^1)-C(O)-OR^1, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)alkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)heteroalkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)alkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-

C_6)cycloalkyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)cycloalkyl, -(C_0-C_6)alkyl-C(O)-O-(C_1-C_6)heterocyclyl, -(C_0-C_6)heteroalkyl-C(O)-O-(C_1-C_6)heterocyclyl, -(C_0-C_6)alkyl-C(O)-$N(R^1)_2$, -(C_0-C_6)heteroalkyl-C(O)-$N(R^1)_2$ and -C(O)-$N(R^1)$-C_2-C_6alkyl-W, wherein each aryl, heteroaryl, cycloalkyl or heterocyclyl moiety is optionally substituted with one or more groups selected from R^2; wherein

M is selected from the group consisting of CH_2, O, S, S(O), $S(O)_2$ and $N(R^1)$; or

C and D together with the carbon atom to which they are attached form a (C_3-C_6)cycloalkyl, wherein the cycloalkyl is optionally substituted;

R^2 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_0-C_6)alkyl-OR^1, -(C_0-C_6)heteroalkyl-OR^1, -(C_0-C_6)alkyl-C(O)-OR^1, -(C_0-C_6)heteroalkyl-C(O)-OR^1, -CH=CH-C(O)-OR^1, -C≡C-C(O)-OR^1, -CH=CH-C(O)-$N(R^1)_2$, -C≡C-C(O)-$N(R^1)_2$, -$N(R^1)$-C(O)-CF_3, -C(O)-$N(R^1)$-CF_3, -$N(R^1)$-(C_1-C_6)alkyl-$N(R^1)_2$, -$N(R^1)$-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -(C_0-C_6)alkyl-$N(R^1)_2$, -(C_0-C_6)heteroalkyl-$N(R^1)_2$, -$N(R^1)$-C(O)-(C_1-C_6)alkyl, -C(O)-$N(R^1)$-(C_1-C_6)alkyl, -$N(R^1)$-C(O)-(C_1-C_6)heteroalkyl, -C(O)-$N(R^1)$-(C_1-C_6)heteroalkyl, -$N(R^1)$-$S(O)_2$-(C_1-C_6)alkyl, -$N(R^1)$-$S(O)_2$-(C_1-C_6)heteroalkyl, -$S(O)_2$-$N(R^1)$-(C_1-C_6)alkyl, -$S(O)_2$-$N(R^1)$-(C_1-C_6)heteroalkyl, -O-(C_1-C_6)alkyl-$N(R^1)_2$, -O-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -S-(C_1-C_6)alkyl-$N(R^1)_2$, -S-(C_1-C_6)heteroalkyl-$N(R^1)_2$, -S-R^1, -S(O)-(C_1-C_6)alkyl, -S(O)-(C_1-C_6)heteroalkyl, -$S(O)_2$-(C_1-C_6)alkyl, -$S(O)_2$-(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, halo, -CF_3, -OCF_3, -$C(Ph)_3$, -CN, -(C_1-C_6)alkylaryl, aryl, heteroaryl, -(C_1-C_6)alkylheteroaryl, -(C_1-C_6)heteroalkylaryl, -(C_1-C_6)heteroalkylheteroaryl, and -(C_1-C_6)alkyl substituted with a moiety selected from the group consisting of halo, -OH, -NO_2, -(C_0-C_6)alkyl-C(O)-$N(R^1)_2$ and -(C_0-C_6)heteroalkyl-C(O)-$N(R^1)_2$;

A and B are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, heterocyclyl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)heteroalkyl-aryl, -(C_0-C_6)hetroalkyl-heteroaryl, -$S(O)_2$-(C_0-C_6)alkyl-aryl, -$S(O)_2$-(C_0-C_6)alkyl-heteroaryl, -$S(O)_2$-(C_0-C_6)heteroalkyl-aryl, -$S(O)_2$-(C_0-C_6)heteroalkyl-heteroaryl, -C(O)-(C_1-C_6)alkyl-aryl, -C(O)-(C_1-C_6)alkyl-heteroaryl, -C(O)-(C_1-C_6)heteoralkyl-aryl, -C(O)-(C_1-C_6)heteroalkyl-heteroaryl, -C(O)O-(C_0-C_6)alkyl-aryl, -C(O)O-(C_1-C_6)alkyl-heteroaryl, -C(O)O-(C_1-C_6)heteroalkyl-aryl, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl, -C(O)N(R^1)-(C_1-C_6)alkyl-aryl, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-aryl, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl, -(C_2-C_6)alkyl-$N(R^1)_2$, -(C_2-C_6)heteroalkyl-$N(R^1)_2$, -(C_2-C_6)alkyl-O(R^1), -(C_2-C_6)heteroalkyl-O(R^1), -(C_1-C_7)alkyl-W, -(C_1-C_7)heteoralkyl-W, -(C_2-C_5)alkyl-(CH=CH)$_{0-1}$-W, -(C_2-C_5)heteroalkyl-(CH=CH)$_{0-1}$-W, -(C_2-C_5)alkyl-(C≡C)$_{0-1}$-W, -(C_2-C_5)heteroalkyl-C≡C-W, -C(O)-(C_1-C_7)alkyl-W, -C(O)-(C_1-C_7)heteroalkyl-W, -$S(O)_2$-(C_1-C_6)alkyl-W, -$S(O)_2$-(C_1-C_6)heteroalkyl-W, -(C_0-C_7)alkyl-aryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-aryl-(CH=CH)$_{0-1}$-W, -(C_0-C_7)alkyl-aryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)heteroalkyl-aryl-(C≡C)$_{0-1}$-W, -(C_0-C_7)alkyl-

heteroaryl-(CH=CH)$_{0-1}$-W, -(C$_0$-C$_7$)heteroalkyl-heteroaryl-(CH=CH)$_{0-1}$-W, -(C$_0$-C$_7$)alkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C$_0$-C$_7$)heteroalkyl-heteroaryl-(C≡C)$_{0-1}$-W, -(C$_0$-C$_7$)alkyl-aryl-(C$_0$-C$_4$)alkyl-W, -(C$_0$-C$_7$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-W, -(C$_0$-C$_7$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-W, -(C$_0$-C$_7$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-W, -(C$_0$-C$_7$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-W, -(C$_0$-C$_7$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-W, -(C$_0$-C$_7$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-W, -(C$_0$-C$_7$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -S(O)$_2$-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W , -C(O)-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W , -C(O)O-(C$_0$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)alkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)heteroalkyl-aryl-(C$_0$-C$_4$)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_0$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)alkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_1$-C$_6$)alkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_1$-C$_6$)heteroalkyl-heteroaryl-(C$_0$-C$_4$)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)O-(C$_1$-

C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)O-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_0-C_6)alkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_0-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_0-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)alkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)alkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R_1)-(C_1-C_6)heteroalkyl-aryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(CH=CH)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)alkyl-(C≡C)$_{0-1}$-W, -C(O)N(R^1)-(C_1-C_6)alkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W and -C(O)N(R^1)-(C_1-C_6)heteroalkyl-heteroaryl-(C_0-C_4)heteroalkyl-(C≡C)$_{0-1}$-W;

wherein each of the alkyl and heteroalkyl moieties is optionally substituted; and

wherein each of the aryl, heteroaryl, cycloalkyl or heterocyclyl moieties is optionally substituted with one or more groups selected from R^2; and

the asterick mark * indicates a chiral carbon atom,

with the proviso that no more than two of Z, A, B, D and E end with the moiety W.

2. The compound according to claim 1, wherein n is 0.

3. The compound according to claim 1, wherein n is 1.

4. The compound according to claim 1, wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH and C-Z, wherein no more than one of X^1, X^2, X^3 and X^4 are C-Z.

5. The compound according to claim 1, wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, N and C-Z, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z, wherein Z is selected from the group consisting of -H, halo, -CF_3, -NO_2, -CN, -(C_0-C_6)alkyl-OR^1, -(C_0-C_6)alkyl-N(R^1)$_2$, -(C_1-C_6)alkyl, -N(R^1)-C(O)-(C_1-C_6)alkyl, -N(R^1)-S(O)$_2$-(C_1-C_6)alkyl, -O-(C_2-C_6)alkyl-N(R^1)(R^1), -S-R^1, -(C_0-C_6)alkyl-C(O)-OR^1, -N(R^1)-C(O)-CF_3 or -N(R^1)-(C_2-C_6)alkyl-N(R^1)(R^1), -(C_0-C_7)alkyl-W, -C(O)-N(R^1)-(C_1-C_6)alkyl-W, -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-W, -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-C(O)-aryl, -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-C(O)-heteroaryl, -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-C(O)-N(R^1)-aryl, -(C_0-C_3)alkyl-N(R^1)-C(O)-

$(C_1$-$C_6)$alkyl-C(O)-N(R^1)-heteroaryl, -$(C_0$-$C_7)$alkyl-aryl-W, -$(C_0$-$C_6)$alkyl-OR^1, -N(R^1)-C(O)-OR^1, wherein each of the aryl, heteroaryl, cycloalkyl and heterocyclyl moieties of the above-mentioned Z is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -$(C_1$-$C_6)$alkyl, -$(C_1$-$C_6)$alkoxy, -NO_2, -N$(R^1)_2$, halo, -SH, mono- to per-halogenated-$(C_1$-$C_6)$alkyl and -$(C_2$-$C_4)$alkyl-N$(R^1)_2$, wherein two R^1 groups, together with the nitrogen atom to which they are attached optionally form a heterocyclyl group .

6. The compound according to claim 1, wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH, C-Z and N, wherein no more than two of X^1, X^2, X^3 and X^4 are N and no more than one of X^1, X^2, X^3 and X^4 are C-Z, wherein Z is selected from the group consisting of -F, -Cl, -Br, CF_3, NO_2, -CN, -OR^1, -NR^1R^1, -$(CH_2)_{0-4}$OR^1, -$(CH_2)_{0-4}$N$(R^1)_2$, -CH_2OH, -CH_3, -N(R^1)C(O)CH_3, -N(R^1)SO_2CH_3, -O$(CH_2)_{2-4}$N(R^1)(R^1), -SR^1, -$(CH_2)_{0-4}$C(O)OR^1, -N(R^1)C(O)CF_3 and -N(R^1)$(CH_2)_2$N(R^1)(R^1), wherein two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl group.

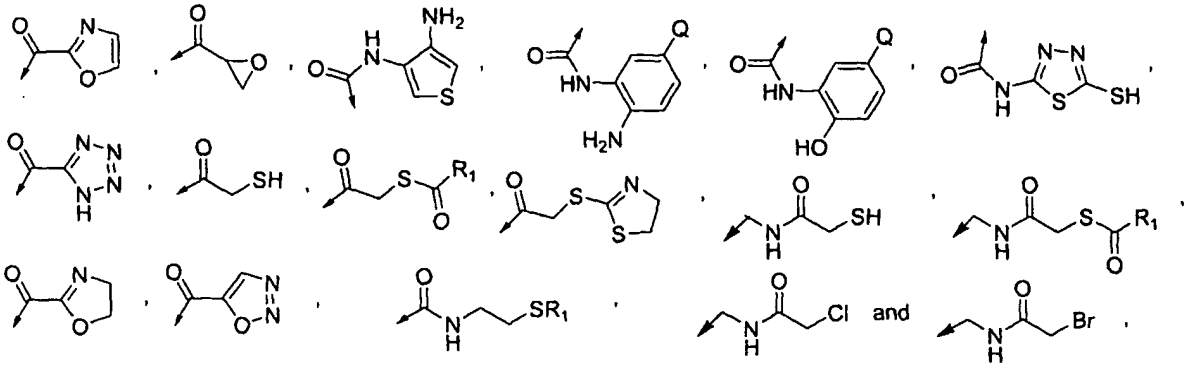
7. The compound according to claim 1, wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of CH and C-Z, wherein only one of X^1, X^2, X^3 and X^4 are C-Z, and wherein Z is selected from the group consisting of -H, -$(C_0$-$C_7)$alkyl-W, -$(C_0$-$C_5)$alkyl-CH=CH-W, -$(C_0$-$C_5)$alkyl-C≡C-W, -C(O)-$(C_1$-$C_7)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-C(S)-$(C_1$-$C_6)$alkyl-W, -C(O)-N(R^1)-$(C_1$-$C_6)$alkyl-W, -C(S)-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-C(S)-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-O-$(C_1$-$C_6)$alkyl-W, -S$(O)_2$-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-N(R^1)-S$(O)_2$-$(C_1$-$C_6)$alkyl-W, -O-C(O)-N$(R^1)_2$, -$(C_0$-$C_6)$alkyl-O-C(O)-N(R^1)-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-O-$(C_1$-$C_6)$alkyl-W, -$(C_0$-$C_3)$alkyl-S-$(C_1$-$C_6)$alkyl-W, -N(R^1)-C(O)-O-S$(O)_2$-N$(R^1)_2$, -N(R^1)-S$(O)_2$-R^1, -$(C_0$-$C_7)$alkyl-aryl-W, -$(C_0$-$C_7)$alkyl-heteroaryl-W, -$(C_0$-$C_3)$alkyl-O-$(C_0$-$C_3)$alkyl-aryl, -$(C_0$-$C_3)$alkyl-O-$(C_0$-$C_3)$alkyl-heteroaryl, -aryl, -$(C_1$-$C_6)$alkylaryl, -heteroaryl, -$(C_1$-$C_6)$alkylheteroaryl, -$(C_1$-$C_8)$heteroalkyl, -$(C_3$-$C_6)$cycloalkyl, -$(C_3$-$C_6)$heterocycloalkyl, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-$(C_1$-$C_6)$alkyl-C(O)-aryl, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-$(C_1$-$C_6)$alkyl-C(O)-heteroaryl, -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-$(C_1$-$C_6)$alkyl-C(O)-N(R^1)-aryl and -$(C_0$-$C_3)$alkyl-N(R^1)-C(O)-$(C_1$-$C_6)$alkyl-C(O)-N(R^1)-heteroaryl, wherein two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl group.

8. The compound according to claim 7, wherein R^1 is independently -$(C_0$-$C_6)$alkyl-aryl or -$(C_1$-$C_4)$alkyl.

9. The compound according to claim 8, wherein R^1 is independently selected from the group consisting of phenyl, benzyl, methyl, ethyl, *t*-butyl and *i*-propyl.

10. The compound according to claim 7, wherein when Z is -(C_2-C_4)alkyl-N(R^1)$_2$ the two R^1 groups, together with the nitrogen atom to which they are attached, optionally form a heterocyclyl selected from the group consisting of morpholinyl, piperazinyl, piperidinyl, pyrrolydinyl, and azetidinyl.

11. The compound according to claim 1, wherein W is selected from the group consisting of



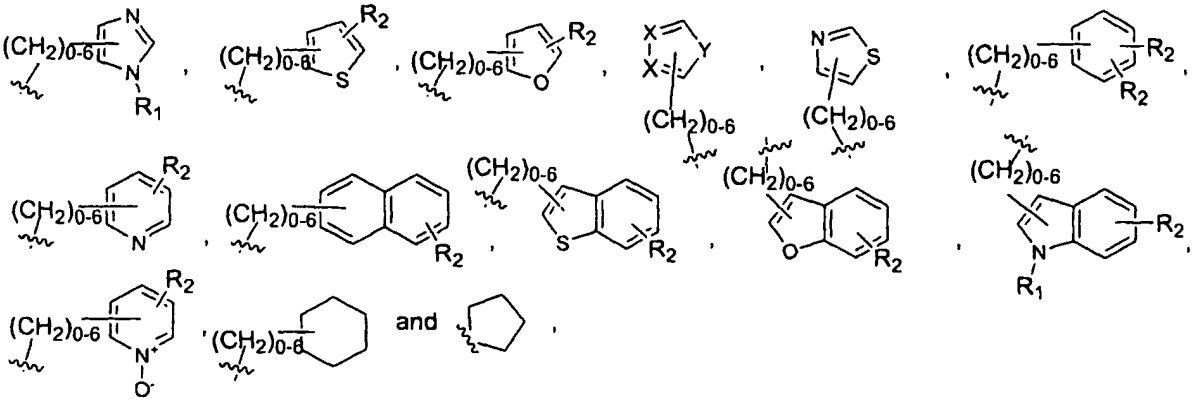
wherein Q is selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-OR^1, heterocyclyl, -N(R^1)$_2$, halo, aryl and heteroaryl;

12. The compound according to claim 1, wherein W is selected from the group consisting of -C(O)-NH-OH, -$COCF_3$, -$COCHF_2$, -$COCH_2F$, -$C(O)CH_3$, -$C(O)C_2H_5$, -$(CH_2)_{1-6}$-N(OH)C(O)H and -$CON(R^1)_2$.

13. The compound according to claim 1, wherein Q is independently selected from the group consisting of heterocyclyl, aryl and heteroaryl.

14. The compound according to claim 13, wherein Q is independently selected from the group consisting of thiophenyl, furanyl, tetrazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrrolyl, thiazolyl, oxazolyl and isooxazolyl.

15. The compound according to claim 1, wherein E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_1-C_6)alkyl-OR^1, -(C_1-C_6)alkyl-C(O)-N(R^1)$_2$, -(C_1-C_6)alkyl-C(O)-O-(C_1-C_6)alkyl,



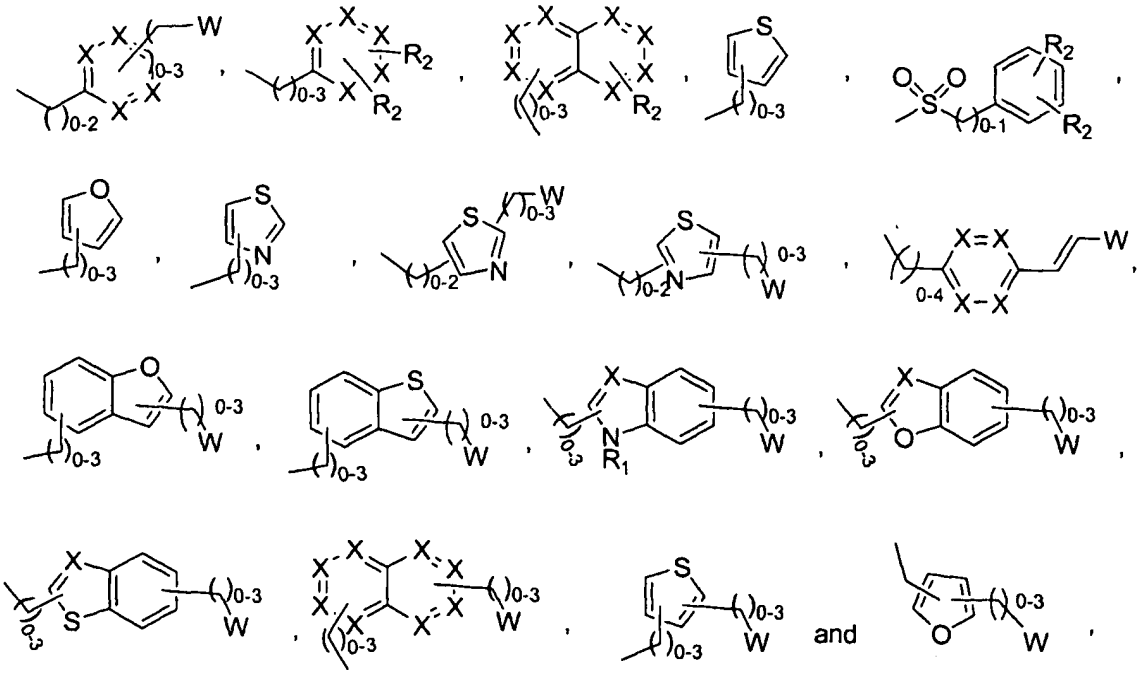
wherein Y is selected from the group consisting of -O-, -NR^1-, and -S-, and X is -CH- or -N-.

16. The compound according to claim 1, wherein E and D together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl wherein the cycloalkyl is optionally substituted.

17. The compound according to claim 1, wherein R^2 is independently selected from the group consisting of -H, $-CH_3$, $-OR_1$, $-(CH_2)_{0-4}N(R_1)_2$, -F, -Cl, -Br, $-OCF_3$, $-CF_3$, $-C(Ph)_3$, NO_2, alkyl, aryl, heteroaryl, SR_1 and -CN.

18. The compound according to claim 1, wherein A and B are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, heteroalkyl, -(C_3-C_6)cycloalkyl, heterocycle, -(C_0-C_3)alkyl-aryl, -(C_0-C_3)alkyl-heteroaryl, $-(CH_2)_{1-5}$-W, $-S(O)_2-(CH_2)_{0-5}$-aryl, $-S(O)_2-(CH_2)_{0-5}$-heteroaryl and -C(O)-R^2;
wherein each of the alkyl and heteroalkyl moieties is optionally substituted; and
wherein each of the aryl and heteroaryl moieties is optionally substituted with one or more moieties selected from the group consisting of -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_1-C_6)alkyl, halo, -OH, -O-(C_1-C_6)alkyl, -C(O)OH, -C(O)-NH-OH.

19. The compound according to claim 1, wherein A and B are independently selected from the group consisting of -H,



wherein X is -CH- or -N-.

20. The compound according to claim 1, wherein
X^1, X^3 and X^4 are CH;

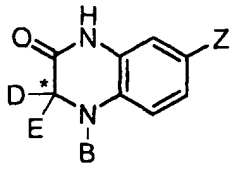
X^2 is C-Z;

n is 0; and

A is -H,

with the proviso that one of E or D is H.

21. The compound according to claim 20, of the formula (II)



(II)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein

Z is selected from the group consisting of -H, $-C(O)-N(R^1)_2$, $-C(O)-N(R^1)-(C_1-C_6)$alkyl-W, $-(C_0-C_7)$alkyl-W, $-(C_2-C_7)$alkenyl-W, $-(C_0-C_3)$alkyl-$N(R^1)-C(O)-(C_1-C_6)$alkyl-W and $-(C_0-C_7)$alkyl-aryl-W;

B is selected from the group consisting of -H, $-S(O)_2-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-heteroaryl and $-(C_0-C_7)$alkyl-aryl-$(CH=CH)_{0-1}$-W; and

E and D are independently selected from the group consisting of -H, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$heteroalkyl, $-(C_0-C_6)$alkyl-aryl, $-(C_0-C_6)$alkyl-heteroaryl, $-(C_0-C_6)$alkyl-W, $-(C_0-C_6)$alkyl-$C(O)-N(R^1)_2$, wherein each of the aryl and heteroaryl is optionally substituted with one or more groups selected from R^2,

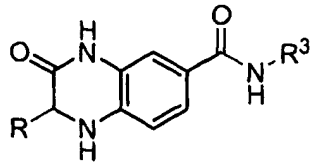
with the proviso that one of E and D is -H.

22. The compound according to claim 21, or a pharmaceutically acceptable salt thereof, wherein

Z is selected from the group consisting of $-C(O)-N(R^1)_2$, $-C(O)-N(R^1)-(C_1-C_6)$alkyl-W; and

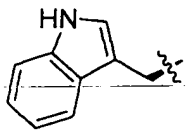
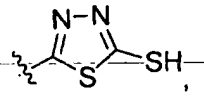
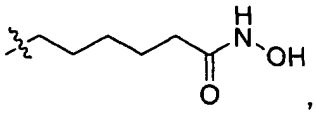
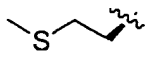
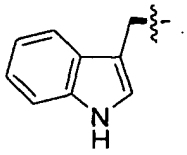
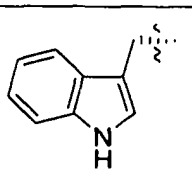
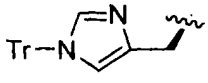
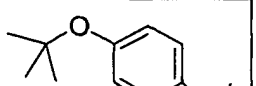
B is -H.

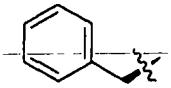
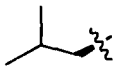
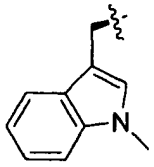
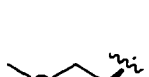
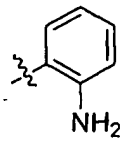
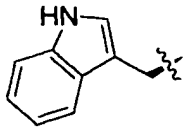
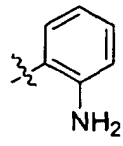
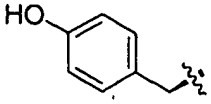
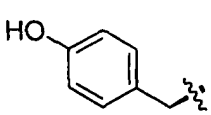
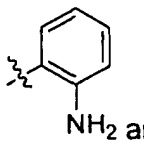
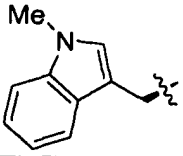
23. The compound according to claim 22, of the formula (III)



(III)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein R and R^3 are a combination selected from the group consisting of:

R	R^3
	 ,
	 ,
	-OH,
	-OH,
	-OH,
	-OH,
	-OH,
	-OH,
	-OH,
	-OH,

R	R^3
	-OH,
H	-OH,
	-OH,
	-OH,
	
	
	-OH,
	
	-OH.

24. The compound according to claim 21, or a pharmaceutically acceptable salt thereof, wherein

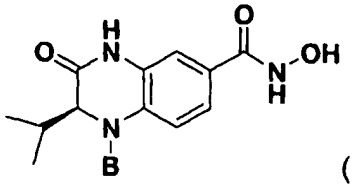
Z is -C(O)-NH-OH;

B is selected from the group consisting of -$S(O)_2$-(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, each of which is optionally substituted and -(C_0-C_7)alkyl-aryl-$(CH=CH)_{0-1}$-W; and

E and D are independently selected from the group consisting of -H and -(C_1-C_6)alkyl, wherein the alkyl moiety is optionally substituted,

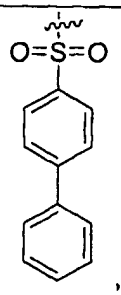
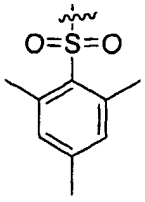
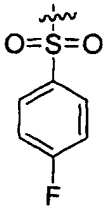
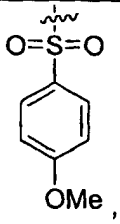
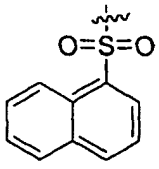
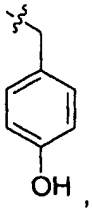
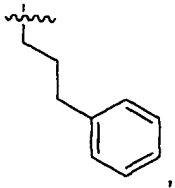
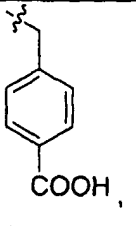
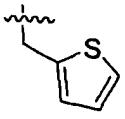
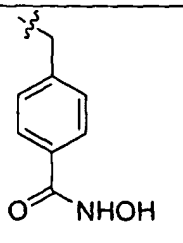
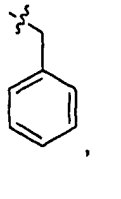
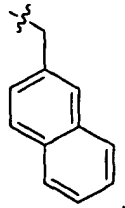
with the proviso that one of C and D is -H.

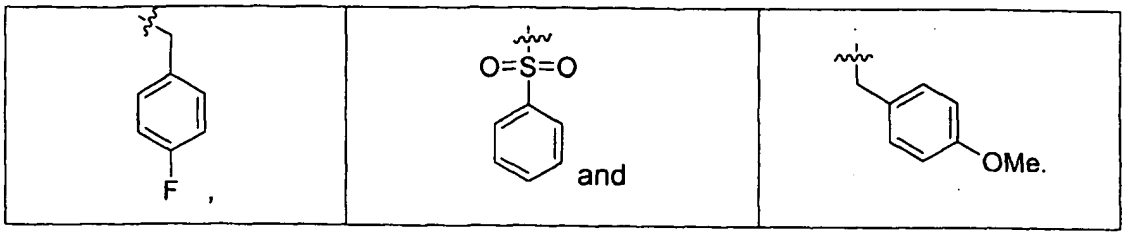
25. The compound according to claim 21, of the formula (IV)



(IV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B is selected from the group consisting of



26. The compound according to claim 1, wherein

n is 0;

X^1, X^3 and X^4 are CH;

X^2 is C-Z;

Z is -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-W;

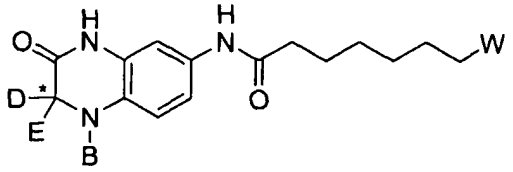
W is selected from the group consisting of -C(O)-NH-OH, -C(O)-heteroaryl, -C(O)-aryl, -C(O)-OR^1, -C(O)-N(R^1)$_2$ and -C(O)-alkyl, wherein the aryl and heteroaryl moieties of said W are optionally substituted;

A is -H;

B is -H or -(C_0-C_6)alkyl-aryl, wherein the aryl moiety is optionally substituted with one or more groups selected from R^2; and

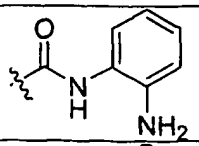
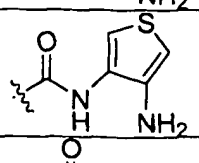
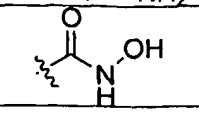
E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl and -(C_0-C_6)alkyl-heteroaryl, wherein the heteroaryl moiety is optionally substituted, with the proviso that at least one of E and D are -H.

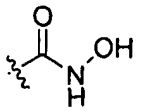
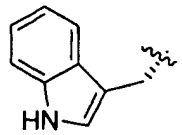
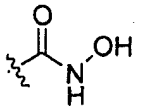
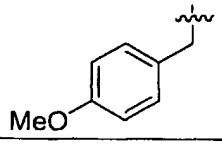
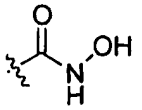
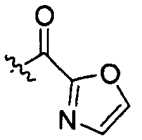
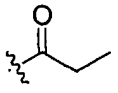
27. The compound according to claim 25, of the formula (V)



(V)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of R and R^4 is selected from the group consisting of

B	E	D	W
H		H	
H		H	
H		H	

H	H		
H	H		
	H		
H		H	
H		H	

28. The compound according to claim 1, wherein

n is 0;

X^1, X^2, X^3 and X^4 are CH;

A is H;

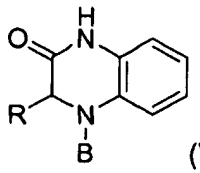
B is selected from the group consisting of -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-aryl-(CH=CH)$_{0-1}$-W, wherein the W moiety is optionally *meta* or *para* to the -(C_0-C_6)alkyl moiety, and wherein the aryl moiety of each of the aforementioned B is optionally substituted with one or more substitutents selected from R^2;

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-NH-aryl, wherein the aryl is optionally substituted,

E and D are independently selected from the group consisting of -H, -(C_1-C_6)alkyl-M-(C_1-C_3)alkyl-W, -(C_0-C_6)alkyl-C(O)-N(R^1)$_2$, -(C_0-C_6)alkyl-heteroaryl, -(C_0-C_6)alkyl-aryl and -(C_1-C_6)alkyl-N(R^1)-C(O)-OR^1; and

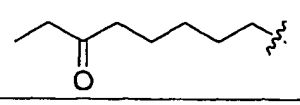
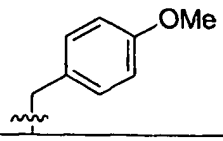
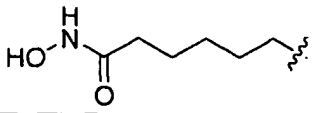
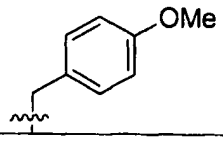
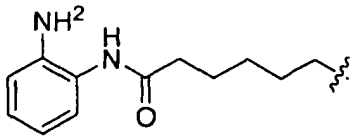
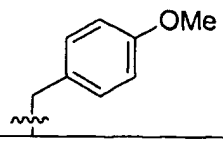
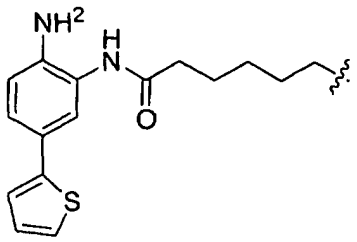
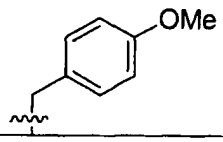
R^1 is independently selected from the group consisting of -H and -(C_1-C_6)alkyl.

29. The compound according to claim 28, of the formula (VI)

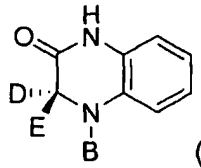


(VI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B and R are a combination selected from the group consisting of

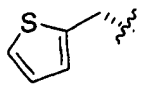
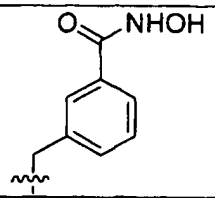
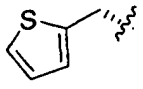
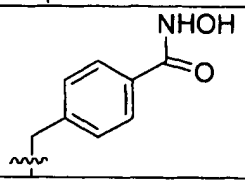
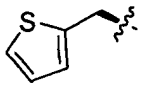
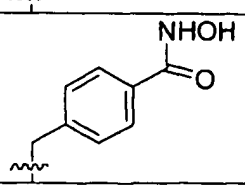
R	B
	
	
	
	

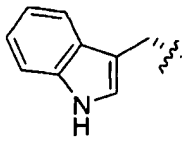
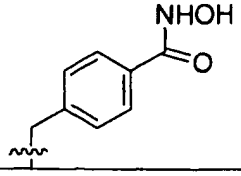
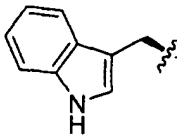
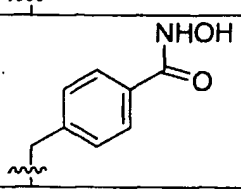
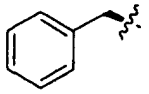
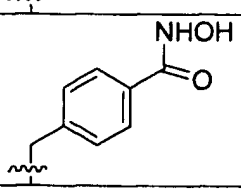
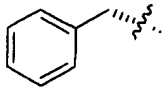
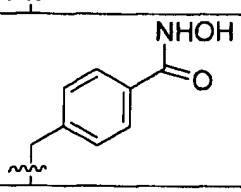
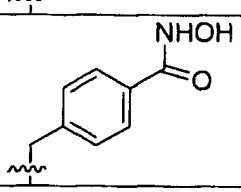
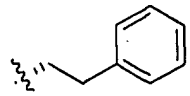
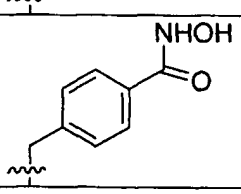
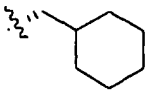
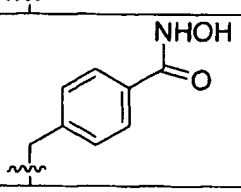
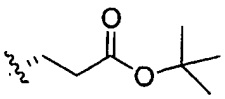
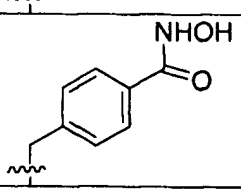
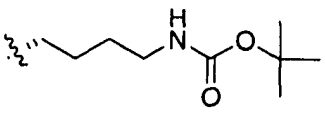
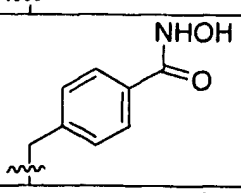
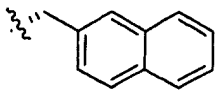
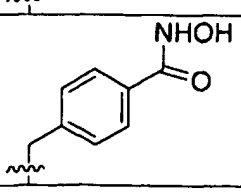
30. The compound according to claim 28, of the formula (VII)

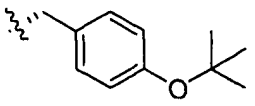
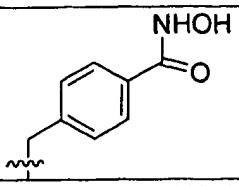
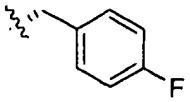
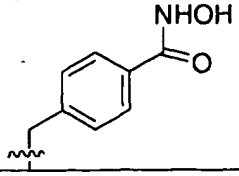
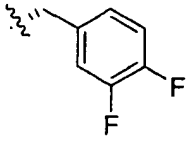
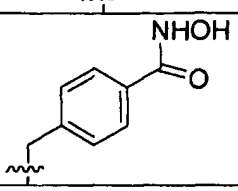
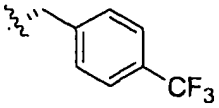
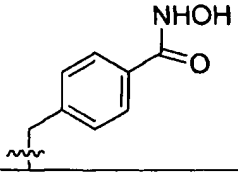
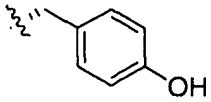
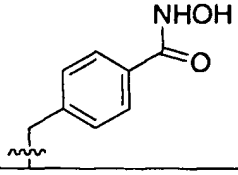
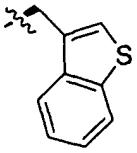
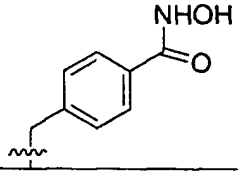
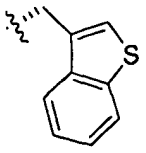
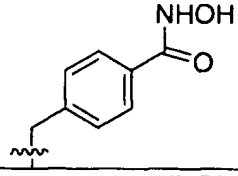
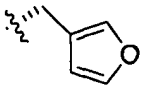
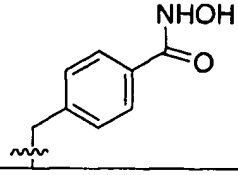
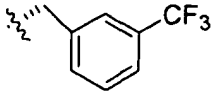
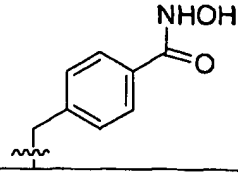
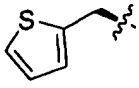
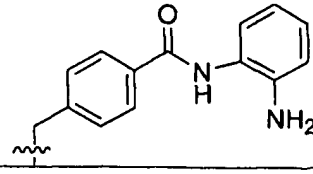


(VII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein B, D and E are a combination selected from the group consisting of

D	E	B
	H	
	H	
H		

D	E	B
	H	
H		
H		
	H	
H	H	
	H	
	H	
	H	
	H	
	H	

D	E	B
	H	
	H	
	H	
	H	
	H	
H		
	H	
	H	
	H	
H		

31. The compound according to claim 1, wherein

n is 0;

X^1, X^2 and X^3 are CH;

X^4 is C-Z;

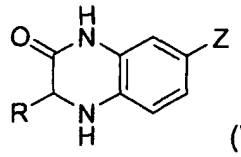
Z is -(C_0-C_7)alkyl-aryl-W;

W is -C(O)-N(R_1)$_2$;

A and B are -H; and

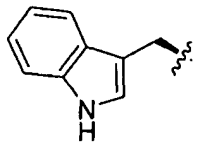
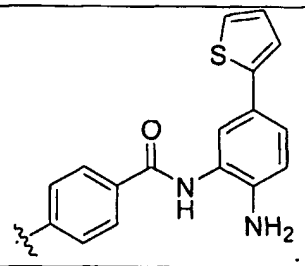
E and D are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-heteroaryl, with the proviso that one of C and D is -H.

32. The compound according to claim 30, of the formula (VIII)



(VIII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of R and Z is selected from the group consisting of

R	Z
	

33. The compound according to claim 1, wherein

n is 0;

X^1, X^2 and X^3 are CH;

X^4 is C-Z;

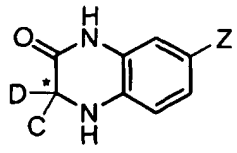
Z is -(C_0-C_7)alkyl-W or -(C_2-C_7)alkenyl-W;

W is -C(O)-NH-OH;

A and B are -H; and

E and D are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-heteroaryl, with the proviso that one of C and D is -H.

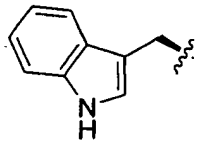
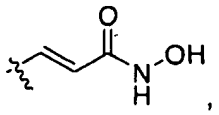
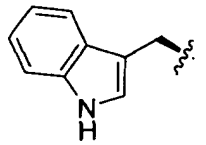
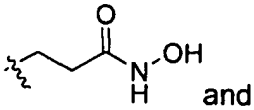
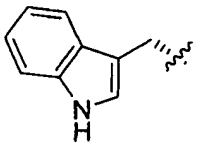
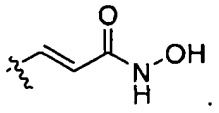
34. The compound according to claim 32, of the formula (IX)



(IX)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of

E, D and Z is selected from the group consisting of

E	D	Z
	H	 ,
	H	 and
H		 .

35. The compound according to claim 1, wherein

n is 1;

X^1 and X^4 are CH;

X^2 and X^3 are C-Z;

Z is selected from the group consisting of -H, -(C_0-C_7)alkyl-W, -(C_0-C_6)alkyl-OR^1, -$N(R^1)$-C(O)-OR^1 and -(C_0-C_3)alkyl-$N(R^1)$-C(O)-(C_1-C_6)alkyl-W;

A is selected from the group consisting of -H and -(C_1-C_7)alkyl-W, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, wherein the aryl and heteoraryl moiety are optionally substituted with one or more substituents selected from the group consisting of R^2;

B is -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl, -(C_1-C_6)alkyl-heteroaryl, -(C_1-C_6)alkyl-W, wherein each of the cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2;

W is independently selected from the group consisting of -C(O)-NH-OH, -C(O)-OR^1, -C(O)-$N(R^1)_2$;

R^1 is independently selected from the group consisting of -H and -(C_0-C_6)-alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, -(C_1-C_6)-alkyl wherein each of the aryl and heteroaryl moieties is optionally substituted; and

R^2 is selected from the group consisting of -(C_0-C_6)alkyl substituted with halo, -(C_0-C_6)alkyl-OR_1, -(C_1-C_7)alkyl-W.

36. The compound according to claim 35, wherein

X^1, X^2, X^3 and X^4 are CH;

A is selected from the group consisting of -(C_1-C_7)alkyl-W;

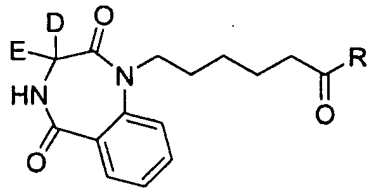
D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl, -(C_1-C_6)alkyl-heteroaryl, wherein each of the cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2;

W is independently selected from the group consisting of -C(O)-NH-OH, -C(O)-OR^1, -C(O)-$N(R^1)_2$;

R^1 is independently selected from the group consisting of -H, -(C_0-C_6)-alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl, wherein each of the aryl and heteroaryl moieties is optionally substituted; and

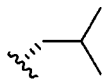
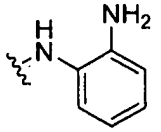
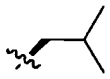
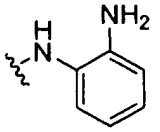
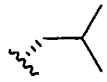
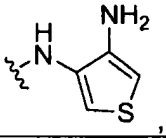
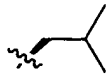
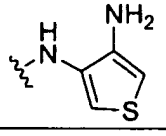
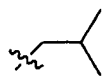
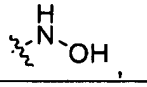
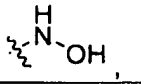
R^2 is selected from the group consisting of -(C_0-C_6)alkyl-OR_1.

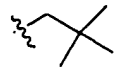
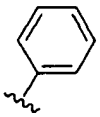
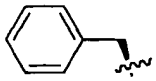
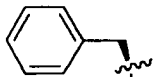
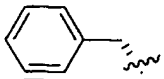
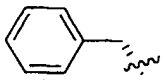
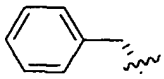
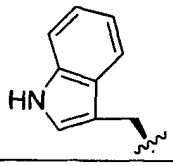
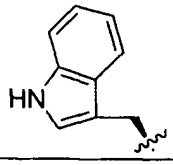
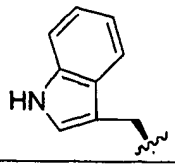
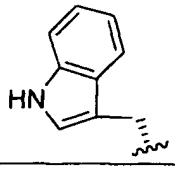
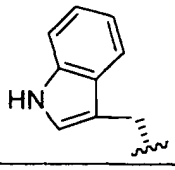
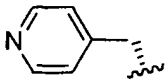
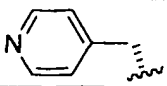
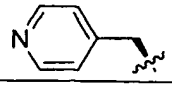
37. The compound according to claim 36, of the formula (X)

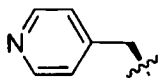
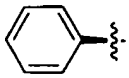
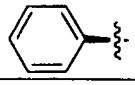
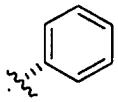
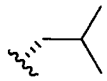
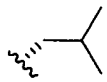
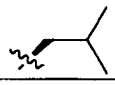
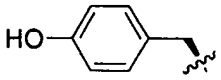
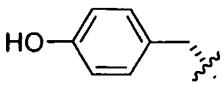
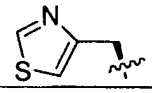
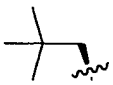
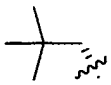
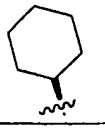
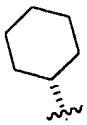
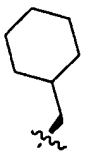
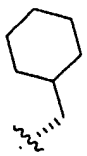


(X)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein D, E and R are a combination selected from the group consisting of

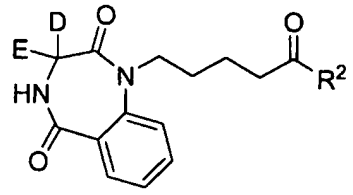
D	E	R
	H	
H		
	H	
H		
	H	
H	H	

D	E	R
	H	 ,
	H	 ,
H		-OH ,
H		-NH-OH
	H	 ,
	H	-OH ,
	H	-NH-OH ,
H		 ,
H		-OH ,
H		-NH-OH ,
	H	-OH ,
	H	-NH-OH ,
	H	-OH ,
	H	-NH-OH ,
H		-OH ,

D	E	R
H		-NH-OH ,
H		-OH ,
H		-NH-OH ,
	H	-NH-OH,
	H	-OH ,
	H	-NH-OH ,
H		-NH-OH,
H		-OH ,
	H	-OH ,
H		-OH ,
		-NH-OH ,
H		-NH-OH ,
	H	-NH-OH ,
H		-NH-OH ,
	H	-NH-OH,
H		-NH-OH ,
	H	-NH-OH ,

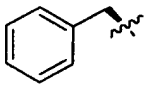
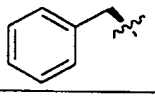
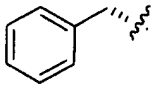
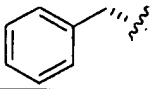
D	E	R
H		-NH-OH and
	H	-NH-OH.

38. The compound according to claim 36, of the formula (XI)



(XI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein D, E and R are a combination selected from the group consisting of

D	E	R
H		 ,
H		-OH,
	H	 and
	H	-OH.

39. The compound according to claim 35, wherein

X^1, X^2, X^3 and X^4 are CH;

A is selected from the group consisting of -H, -(C_0-C_6)alkyl-aryl, -(C_0-C_6)alkyl-heteroaryl, wherein the aryl and heteoraryl moiety are optionally substituted with one or more substituents selected from the group consisting of R^2;

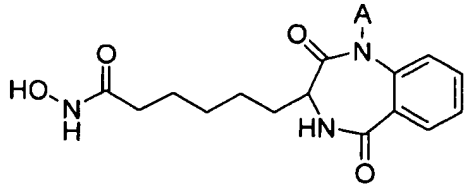
B is -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl-W;

W is -C(O)-NH-OH; and

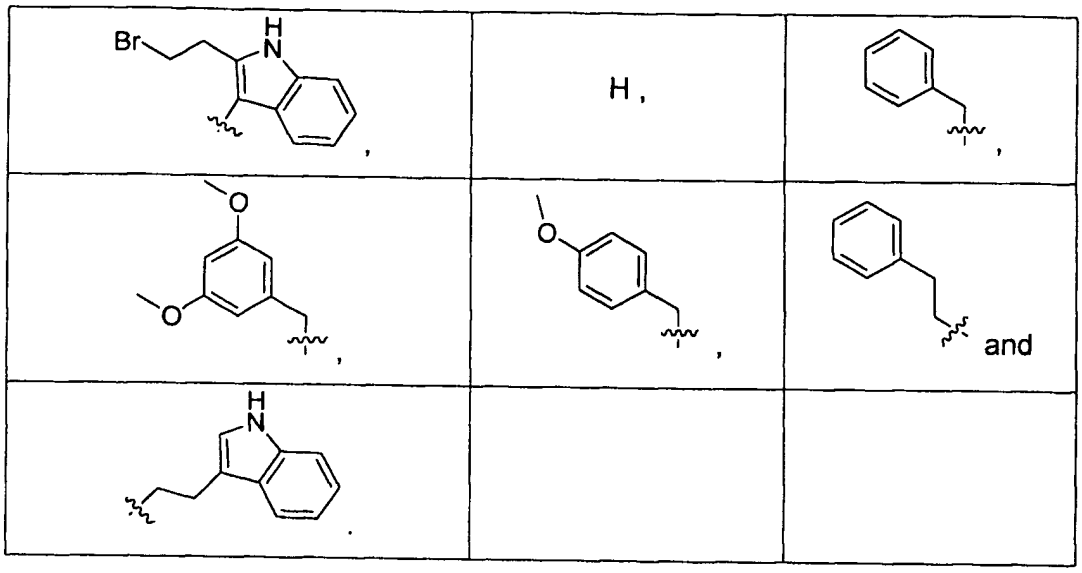
R^2 is selected from the group consisting of -(C_0-C_6)alkyl substituted with halo and -(C_0-C_6)alkyl-OR_1.

40. The compound according to claim 39, of the the formula (XII)



(XII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein A is selected from the group consisting of



41. The compound according to claim 35, wherein

X^1, X^2 and X^4 are CH;

X^3 is C-Z;

Z is -(C_0-C_6)alkyl-OR^1;

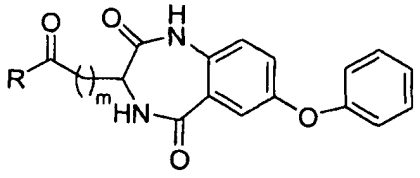
R^1 is -(C_0-C_6)alkyl-aryl;

A is -H;

D and E are independently selected from the group consisting of -H and -(C_1-C_6)alkyl-W; and

W is -C(O)-NH-OH and -C(O)-OR^1.

42. The compound according to claim 41, of the formula (XIII)



(XIII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of m and R is selected from the group consisting of

m	R
1	-NH-OH
2	-NH-OH
5	-NH-OH
1	-OH
2	-OH
4	-OH

43. The compound according to claim 35, wherein

X^1, X^2 and X^4 are CH;

X^3 is C-Z;

Z is selected from the group consisting of -N(R^1)-C(O)-OR^1 and -(C_0-C_3)alkyl-N(R^1)-C(O)-(C_1-C_6)alkyl-W;

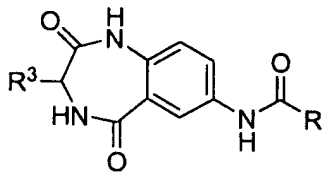
A and B are -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl and -(C_1-C_6)alkyl-W;

W is independently selected from the group consisting of -C(O)-NH-OH and -C(O)-OR^1; and

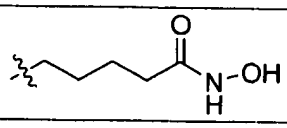
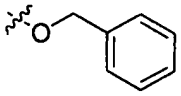
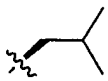
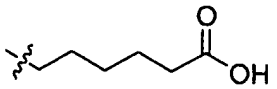
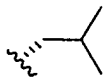
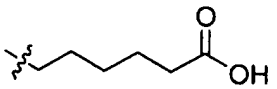
R^1 is independently selected from the group consisting of -H and -(C_0-C_6)-alkyl-aryl, wherein the aryl moiety is optionally substituted.

44. The compound according to claim 43, of the formula (XIV)



(XIV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein the combination of D, E and R is selected from the group consisting of

R^3	R
	
	
	

45. The compound according to claim 35, wherein

X^1, X^3 and X^4 are CH;

X^2 is C-Z;

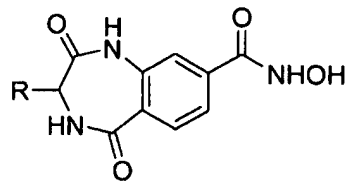
Z is -(C_0-C_7)alkyl-W;

A and B are -H;

D and E are independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_0-C_6)alkyl-(C_3-C_6)cylcoalkyl, -(C_0-C_6)alkyl-aryl and -(C_1-C_6)alkyl-heteroaryl, wherein each of the cylcoalkyl, aryl and heteroaryl moieties is optionally substituted with one or more groups selected from R^2; and

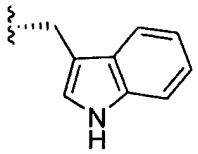
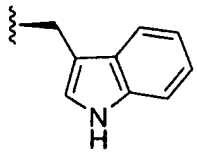
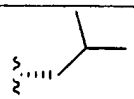
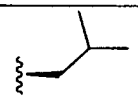
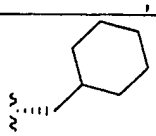
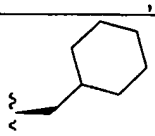
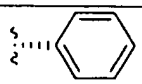
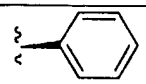
W is -C(O)-NH-OH.

46. The compound according to claim 45, of the formula (XV)



(XV)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein R is selected from the group consisting of

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 and
H.	

47. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-tetrahydro-N-hydroxy-2-(2-(methylthio)ethyl)-3-oxoquinoxaline-6-carboxamide,
(S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(S)-2-sec-butyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(R)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
(R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-tetrahydro-N-hydroxy-3-oxo-2-((1-trityl-1H-imidazol-4-yl)methyl)quinoxaline-6-carboxamide,
(S)-2-(4-tert-butoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(S)-2-Benzyl-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-Tetrahydro-N-hydroxy-2-isobutyl-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-tetrahydro-N-hydroxy-2-((1-methyl-1-H-indol-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide,

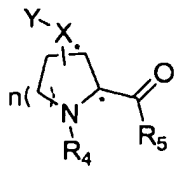
(S)-2-((1H-indol-3-yl)methyl)-N-(2-aminophenyl)-1,2,3,4-tetrahydro-3-oxoquinoxaline-6-carboxamide,
(S)-2-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-3-oxoquinoxaline-6-carboxamide,
(S)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3 oxoquinoxaline-6-carboxamide,
(S)-N-(5-(Hydroxycarbamoyl)pentyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
(S)-1-(4-fluorobenzyl)-N-hydroxy-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-1-(4-hydroxybenzyl)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-(3-phenylpropyl)quinoxaline-6-carboxamide,
4-(((S)-7-(hydroxycarbamoyl)-2,3-dihydro-3-isopropyl-2-oxoquinoxalin-4(1H)-yl)methyl)benzoic acid,
(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxo-1-((thiophen-2-yl)methyl)quinoxaline-6-carboxamide,
(S)-N-hydroxy-1-(4-(N-hydroxycarbamimidoyl)benzyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-1-benzyl-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-3-oxoquinoxaline-6-carboxamide,
(S)-1,2,3,4-tetrahydro-N-hydroxy-2-isopropyl-1-((naphthalen-3-yl)methyl)-3-oxoquinoxaline-6-carboxamide,
(S)-N-hydroxy-2-isopropyl-3-oxo-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-N-hydroxy-1-(biphenyl-4-sulfonyl)-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-N-hydroxy-2-isopropyl-3-oxo-1-(2,4,6-trimethybenzenesulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-N-hydroxy-1-(4-methoxybenzenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
(S)-N-hydroxy-1-(1-naphthalenesulfonyl-2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide,
N1-(2-Aminophenyl)-N8-((S)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)octanediamide,
N1-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
N1-((R)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
N1-((R)-2-((1H-Indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
N1-((R)-1-(4-Methoxybenzyl)-1,2,3,4-tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-N8-hydroxyoctanediamide,
N-((S)-1,2,3,4-Tetrahydro-2-isopropyl-3-oxoquinoxalin-6-yl)-8-(oxazol-2-yl)-8-oxooctanamide,
6-((R)-1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxy-4-oxy-hexanamide,
6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-hydroxyhexanamide,
6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-aminophenyl)hexanamide,
6-(1-(4-methoxybenzyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-2-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)hexanamide,

4-(((S)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-benzamide,
(R)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(S)-4-((2-((1H-indol-3-yl)methyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(S)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-4-((2-benzyl-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
N-hydroxy-4-((3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(R)-N-hydroxy-4-((3-oxo-2-phenethyl-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(R)-4-((2-(cyclohexylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-tert-butyl 4-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)butylcarbamate,
(R)-N-hydroxy-4-((2-(naphthalen-2-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(R)-4-((2-(4-tert-butoxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-tert-butyl 3-(1-(4-(hydroxycarbamoyl)benzyl)-3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)propanoate,
(R)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(S)-4-((2-(benzo[b]thiophen-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-4-((2-(4-fluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-4-((2-(3,4-difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-4-((2-(4-trifluoromethylbenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-N-hydroxy-4-((2-(4-hydroxybenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(R)-N-hydroxy-4-((2-(3-(trifluoromethyl)benzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(R)-4-((2-(furan-3-ylmethyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)-N-hydroxybenzamide,
(R)-N-hydroxy-4-((3-oxo-2-(pyridin-3-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
(S)-N-(2-aminophenyl)-4-((3-oxo-2-(thiophen-2-ylmethyl)-3,4-dihydroquinoxalin-1(2H)-yl)methyl)benzamide,
4-(((R)-2,3-Dihydro-2-oxo-3-((thiophen-2-yl)methyl)quinoxalin-4(1H)-yl)methyl)-N-hydroxybenzamide,
4-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-(2-amino-5-(thiophen-2-yl)phenyl)benzamide,
(E)-3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide,

(E)-3-((R)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxyacrylamide,
6-((S)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-3-((1H-indol-3-yl)methyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-2,5-dioxo-3-((pyridin-4-yl)methyl)benzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-2,3,4,5-tetrahydro-2,5-dioxo-3-phenylbenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-(3,3-spirocyclopentyl-2,5-dioxo-2,3,4,5,tetrahydrobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-3-neopentyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-3-cyclohexyl-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((S)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
6-((R)-2,3,4,5-tetrahydro-3-methyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide,
3-((S)-2-((1H-indol-3-yl)methyl)-1,2,3,4-tetrahydro-3-oxoquinoxalin-6-yl)-N-hydroxypropanamide,
N-(2-aminophenyl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide,
N-(4-aminothiophen-3-yl)-6-((R)-2,3,4,5-tetrahydro-3-isobutyl-2,5-dioxobenzo[e][1,4]diazepin-1-yl)hexanamide,
6-(2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(1-(2-(1H-indol-3-yl)ethyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(1-benzyl-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(1-(3,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,

6-(1-(4-methoxybenzyl)-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(2,3,4,5-tetrahydro-2,5-dioxo-1-phenethyl-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(2,3,4,5-tetrahydro-2,5-dioxo-7-phenoxy-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
6-(7-Benzyloxycarbonylamino-2,3,4,5-tetrahydro-2,5-dioxo-1H-benzo[e][1,4]diazepin-3-yl)-N-hydroxyhexanamide,
(S)-benzyl 3-(6-(hydroxyamino)-6-oxohexyl)-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepin-7-ylcarbamate,
(R)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(S)-N-hydroxy-3-isopropyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(S)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(R)-3-((1H-indol-3-yl)methyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(R)-N-hydroxy-3-isobutyl-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(R)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(S)-3-(cyclohexylmethyl)-N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(S)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(R)-N-hydroxy-2,5-dioxo-3-phenyl-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
N-hydroxy-2,5-dioxo-2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepine-8-carboxamide,
(R)-2-(4-((2-(3,4-Difluorobenzyl)-3-oxo-3,4-dihydroquinoxalin-1(2H)-yl)methyl)phenyl)-N-hydroxyacetamide,
(R)-2-(3,4-Difluorobenzyl)-N-(4-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide,
(R)-2-(3,4-difluorobenzyl)-N-(3-(hydroxycarbamoyl)phenyl)-3-oxo-3,4-dihydroquinoxaline-1(2H)-carboxamide,
(2S,4S)-Benzyl 4-(5-(hydroxycarbamoyl)pyrimidin-2-ylamino)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(R)-4-((2-((1H-Indol-3-yl)methyl)-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxybenzamide,
(R)-4-((2-Benzyl-3,6-dioxopiperazin-1-yl)methyl)-N-hydroxybenzamide,
(R)-4-((3,6-Dioxo-2-(thien-2-ylmethyl)piperazin-1-yl)methyl)-N-hydroxybenzamide and
6-(2,3,4,5-tetrahydro-2,5-dioxobenzo[e][1,4]diazepin-1-yl)-N-hydroxyhexanamide.

48. A compound of the formula XVI,



(XVI)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein

n is 1 or 2;

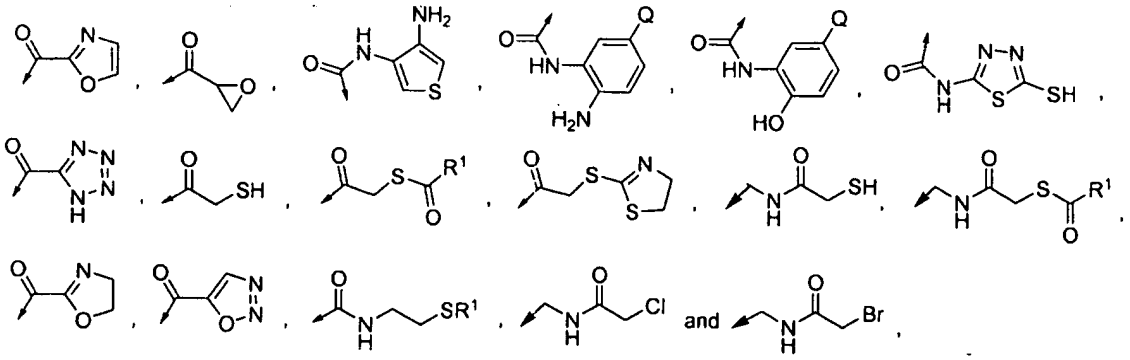
X is selected from the group consisting of -O-, -S-, -N(R^1)- and -CH(R^1)-;

Y is selected from the group consisting of -(C_0-C_7)alkyl-heteroaryl-W, -(C_1-C_7)alkyl-W, -(C_0-C_7)alkyl-aryl-W and -C(O)-(C_1-C_7)alkyl-W;

W is selected from the group consisting of -C(O)-NH-OH, -C(O)-(C_1-C_4)alkyl, -C(O)-N(R^1)$_2$, -(C_2-C_6)alkyl-N(OH)-C(O)H-, -(C_1-C_6)alkyl-SR^1, -(C_1-C_6)alkyl-SC(O)-(C_1-C_4)alkyl, -C(O)-OR^1, -C(O)-(C_1-C_4)alkylepoxide, -C(O)-(C_1-C_4)alkyl-SH, -C(O)-(C_1-C_4)alkyl-SC(O)R^1, -C(O)-(C_1-C_4)alkyl-S-heteroaryl, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-halo, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SH, -(C_1-C_6)alkyl-NH-C(O)-(C_1-C_6)alkyl-SC(O)R^1, -C(O)-NH-(C_2-C_6)alkyl-SH and -C(O)-(C_1-C_6)alkyl,

wherein the alkyl of said -C(O)-(C_1-C_6)alkyl is optionally substituted with one or more substituents selected from the group consisting of mono to per-halogenated -(C_1-C_6)alkyl, -C(O)-heteroaryl, -C(O)-NH-heteroaryl and -C(O)-NH-aryl;

wherein each aryl and heteroaryl is optionally substituted with one or more substituents selected from the group consisting of -NH_2, -OH, SH, -CN, -NO_2, -N(R^1)$_2$, halo, mono- to per-halogenated-(C_1-C_6)alkyl, aryl, heteroaryl,



wherein Q is selected from the group consisting of heterocyclic, aryl and heteroaryl;

R^1 is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -(C_1-C_6)heteroalkyl, -(C_3-C_6)cycloalkyl, -heterocyclyl, -(C_0-C_6)alkyl-aryl and -(C_0-C_6)alkyl-heteroaryl,

wherein each afore-mentioned R^1 aryl, heteroaryl, cycloalkyl and heterocyclyl moiety is optionally substituted with one or more substituents selected from the group consisting of oxo, -OH, -CN, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -N(R^1)$_2$, halo, -SH, mono- to per-halogenated-(C_1-C_6)alkyl and -(C_2-C_4)alkyl-N(R^1)$_2$,,

wherein optionally the R^1 together with the nitrogen atom to which they are attached form a heterocyclyl group;

R^4 is selected from the group consisting of -$S(O)_2$-(C_1-C_6)alkyl, -$S(O)_2$-(C_1-C_6)heteroalkyl, -$S(O)_2$-(C_1-C_6)aryl, -$S(O)_2$-(C_1-C_6)alkylaryl, -$S(O)_2$-(C_1-C_6)heteroaryl, -$S(O)_2$-(C_1-C_6)arylalkyl, -$S(O)_2$-(C_1-C_6)heterocyclic, -C(O)-(C_1-C_6)alkyl, -C(O)-(C_1-C_6)heteroalkyl, -C(O)-(C_1-C_6)aryl, -C(O)-(C_1-C_6)alkylaryl, -C(O)-(C_1-C_6)heteroaryl, -C(O)-(C_1-C_6)arylalkyl, -C(O)-(C_1-C_6)heterocyclic and -C(O)-OR^1;

R^5 is selected from the group consisting of -OR^1 and -$N(R^1)_2$; and

the asterick mark * indicates a chiral carbon atom.

with the proviso that when X is NR^1, Y is -C(O)-(C_1-C_7)alkyl-W or -$S(O)_2$-(C_1-C_6)alkyl-W.

49. The compound according to claim 48, wherein Q is selected from the group consisting of thiopheneyl, furanyl, tetrazolyl, imidazolyl, pyridinyl and pyrimidinyl.

50. The compound according to claim 49, wherein

n is 1;

X is -O-;

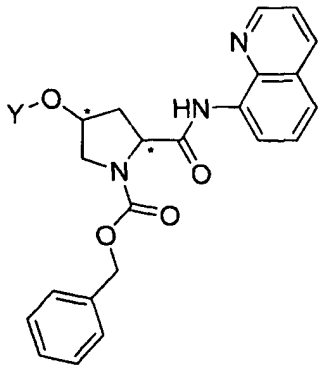
Y is selected from the group consisting of -(C_1-C_7)alkyl-W, -(C_0-C_7)alkyl-aryl-W and -C(O)-(C_1-C_7)alkyl-W;

W is -C(O)-NH-OH;

R^4 is -C(O)-OR^1; and

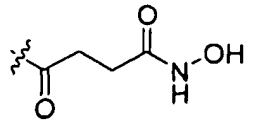
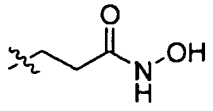
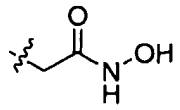
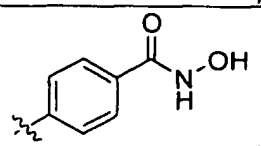
R^5 is -$N(R^1)_2$.

51. The compound according to claim 48, of the formula XVII



(XVII)

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein Y is selected from the group consisting of

 ,	 ,	 and
 .		

52. The compound according to claim 48, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

(2S,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(2S,4R)-benzyl 4-(2-(hydroxyamino)-2-oxoethoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(2R,4R)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(2S,4S)-benzyl 4-(3-(hydroxyamino)-3-oxopropoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(2S,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate,
(2R,4S)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate and
(2S,4R)-benzyl 4-(4-(hydroxycarbamoyl)phenoxy)-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate.

53. The compound according to claim 1, wherein

X^1, X^2, X^3 and X^4 are absent;

X^5 is a covalent bond;

X^6 is CH_2;

n is 1;

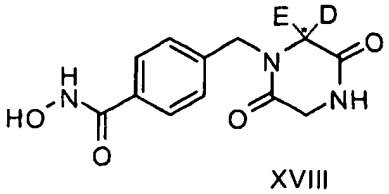
B is -$(C_0$-$C_7)$alkyl-aryl-$(C_0$-$C_4)$alkyl-W;

W is -C(O)NHOH;

A is H; and

E and D are independently selected from a group consisting of -H, -$(C_0$-$C_6)$alkyl-aryl- and -$(C_0$-$C_6)$alkyl-heteroaryl-, wherein each aryl and heteroaryl moiety is optionally substituted with one or more R^2.

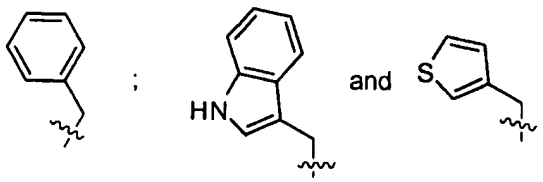
54. The compound according to claim 53, of the formula XVIII



XVIII

and N-oxides, hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof.

55. The compound according to claim 54, wherein one of D and E is H and the other is selected from the group consisting of



, wherein each aryl or heteroaryl moiety is optionally substituted with one or more groups selected from R^2.

56. A composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.

57. A composition comprising a compound according to claim 48 and a pharmaceutically acceptable carrier.

58. A method of inhibiting histone deacetylase, the method comprising contacting the histone deacetylase with an inhibiting effective amount of a compound according to claim 1.

59. A method of inhibiting histone deacetylase, the method comprising contacting the histone deacetylase with an inhibiting effective amount of a compound according to claim 48.

60. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a compound according to claim 1, in an amount sufficient to inhibit histone decetylase.

61. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a compound according to claim 48, in an amount sufficient to inhibit histone decetylase.

62. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a composition according to claim 56, in an amount sufficient to inhibit histone decetylase.

63. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a composition according to claim 57, in an amount sufficient to inhibit histone decetylase.

64. The composition according to claim 56, further comprising an additional histone deacetylase inhibitor.

65. The composition according to claim 57, further comprising an additional histone deacetylase inhibitor.

66. The method according to claim 58, further comprising contacting the cell with an additional histone deacetylase inhibitor in an amount sufficient to inhibit histone decetylase.

67. The method according to claim 59, further comprising contacting the cell with an additional histone deacetylase inhibitor in an amount sufficient to inhibit histone decetylase.

68. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a composition according to claim 64, in an amount sufficient to inhibit histone decetylase.

69. A method of inhibiting histone deacetylase in a cell, the method comprising contacting the cell with a composition according to claim 65, in an amount sufficient to inhibit histone decetylase.

70. The compound according to claim 1, with the proviso that only one of Z, A, B, D and E end in with the moiety W.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2006/001402

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***C07D 243/14*** (2006.01) , ***C07D 241/44*** (2006.01) , ***C07D 207/16*** (2006.01) , ***C07D 401/12*** (2006.01) , ***C07D 403/12*** (2006.01) , ***C07D 409/12*** (2006.01), ***C07D 413/12*** (2006.01) , ***C07D 417/12*** (2006.01)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 8 ***C07D 243/14*** (2006.01) , ***C07D 241/44*** (2006.01) , ***C07D 207/16*** (2006.01) , ***C07D 401/12*** (2006.01) , ***C07D 403/12*** (2006.01) , ***C07D 409/12*** (2006.01), ***C07D 413/12*** (2006.01) , ***C07D 417/12*** (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
CPD (Canadian Patent Database), STN Database, Delphion, Scopus

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 479 348 (SUMITOMO CHEMICAL CO., LTD.) 18 November 1969 (18.11.69) columns 1-5	20
X	WO 04085049 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 7 October 2004 (07.10.04) page 42, scheme 4, final compound	20
X	WO 04018531 (CHEMICAL DIVERSITY RESEARCH INSTITUTE, LTD.) 3 March 2005 (03.03.05) page 71, table 4, compounds 2.1{10}, 2.1{23}	20, 21
X	Li et al., "Comparative study of some synthesised and commercial fluorogenic substrates for horseradish peroxidase and its mimetic enzyme hemin by a flow injection method", Analytica Chimica Acta, 340(1-3), (1997), 159-168 page 160, figure 1, compounds 1-4	20, 21

[x] Further documents are listed in the continuation of Box C. [x] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 November 2006 (29-11-2006)	20 December 2006 (20-12-2006)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Ingrid Popesku 819- 934-2327

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Su et al., "Development of an efficient and selective radioligand for bradykinin B1 receptor occupancy studies", Bioorganic & Medicinal Chemistry Letters, 14(24), (2004), 6045-6048 page 6046, table 1, compounds 1-5	20, 21
X	Morales et al., "Solid-Phase Synthesis of Benzopiperazinones", J. Org. Chem., 63(4), (1998), 1172-1177 page 1173, scheme 2, compounds 7a-e	20-21
X	Nishio, "Photochemical Reactions of Quinoxalin-2-ones and Related Compounds", J. Chem. Soc. Perkin Trans I: Org. & Bioorg. Chem., 3, (1990), 565-570 page 566, compounds 3a-c and 4d	20, 21
E	WO 06102760 (METHYLGENE INC.) 5 October 2006 (05.10.06) page 35; page 71, scheme 5, compounds 74-76; page 77, scheme 7, compounds 89-91; page 85, scheme 12, compounds 111-113; page 186, table 29, compound 503; page 295, table 48, compounds 113, 76, 91, 90; claims 50 and 53	20, 21
X	EP 0 266 102 (PFIZER INC.) 17 March 1993 (17.03.93) pages 5-7, preparations b and e	21
X	US 3 261 828 (HOFFMAN-LA ROCHE INC.) 19 July 1966 (19.07.66) examples 1, 7, 8, 15, 16, 18, 28; claims 1, 2, 7, 8	35
X	Barrow et al., "Spiroquinazoline, a novel substance P inhibitor with a new carbon skeleton, isolated from *aspergillus flavipes*", J. Natural Products, 57(4), (1994), 471-476 page 472, compound 3	35
X	Smith et al., "Solid-phase synthesis of a library of piperazinediones and diazepinediones via kaiser oxime resin", Bioorg. & Med. Chem. Lett., 8(17), (1998), 2369-2374 page 2372, final compound	35
X	Jadidi et al., "Simple synthesis, structure and ab initio study of 1,4-benzodiazepine-2,5-diones", J. Mol. Struc., 692(1-3), (2004), 37-42 page 38, figure 1, compounds 2a-e, 3a	35
X	Akssira et al., "New routes to 1,4-benzodiazepin-2,5-diones", Tetrahedron, 50(30), (1994), 9051-9060 page 9051, scheme 1, compounds 5a, c, 6a, c; page 9054-9055, scheme 3, table 3	35

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2006/001402

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [x] Claim Nos. : 58, 60, 62, 66, 68

because they relate to subject matter not required to be searched by this Authority, namely :

Claims 58, 60, 62, 66 and 68, are directed to a method for treatment of the human or animal body by surgery or therapy which the International Search Authority is not required to search. Regardless, this Authority has carried out a search based on the alleged effects or purposes/uses of the product defined in claims 20-46, 47(in part), 53-55.

2. [x] Claim Nos. : 1-19, 56, 58, 60, 62, 64, 66, 68, 70

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

-see extra sheet

3. [ ] Claim Nos. :

because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

Group A - Claims 1-46, 47 (in part), 53-56, 58, 60, 62, 64, 66, 68, 70 are directed to compounds of formula (I), methods of inhibiting histone deacetylase with the use of the compound of formula (I) and a composition comprising said compound.

Group B - Claims 47 (in part), 48-52, 57, 59, 61, 63, 65, 67, 69 are directed to compounds of formula XVI, methods of inhibiting histone deacetylase with the use of the compound of formula XVI and a composition comprising said compound.

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [x] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. : 1-46, 47 (in part), 53-56, 58, 60, 62, 64, 66, 68, 70

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[x] No protest accompanied the payment of additional search fees.

Continuation of Box II.2:

Claims 1-19, 56, 58, 60, 62, 64, 66, 68, 70 encompass products that are not defined in terms of clear and/or distinguishing technical features as required under Rule 6.3(a) of the PCT. The description provides support within the meaning of Article 6 of the PCT for only a limited number of the products. In the present case, the claims lack clarity and/or support, and a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been established for the parts of the application which appear to be clear and supported, namely claims 20-46, 47 (in part), 53-55.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2006/001402

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